Tech-Watch in Bio-Robotics

Powering Up Paralyzed Muscles – Functional Electrical Stimulation

Latest Technology Innovations Provide a Boost to Stroke Rehabilitation

An Impulse Radio Ultra Wideband System for Contactless Non-invasive Respiratory Monitoring

Diagnosis of Alzheimer’s Disease Using Electric Signals of the Brain – A Grand Challenge
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Call for Contributions: Asia Pacific Biotech News (APBN) is aimed at serving as a platform for providing regional biotechnology and related news as well as a venue for experts in the field to share their views. (Minimum article length: 500 words).

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CONFERENCE CALENDAR
Marrying Robotics and Medicine

This month is the start of something new at APBN. As you’ll see, we’ve combined our October and November issue to lay the foundation for a newer and improved version of APBN to be introduced in 2013. Our website — having undergone a facelift — was the first to be improved. In this month’s issue, we explore the fast-paced domain of robotics. Man’s fascination with robotics begun at the start of the Industrial Revolution and has grown beyond just the manufacturing industry. The possibilities of achievement in robotics are only limited by man’s imagination. However, advancements in robotics have been elusive, and the area is under intense scrutiny — with everyone searching for that one breakthrough technology to shake up the industry. At the forefront of progress in robotics is Japan — a country faced with a rapidly aging population that is picking up the slack in preparation for its graying future. Even car manufacturing tycoon Toyota has a foothold in this area when they recently launched the Human Support Robot (HSR) prototype in addition to last year’s Independent Walk Assist robot.

The reality of artificial intelligence and human-like androids, or humanoids (as Dr. Hiroshi Ishiguro calls them), entering our world as “co-workers” and “caretakers” could soon materialize. In Asia, the decades-long funding of healthcare robots to aid the elderly has culminated with the introduction of telepresence robots in Singapore’s Khoo Teck Puat Hospital and rehabilitative robots for stroke patients by Kinesis.

In an exciting jump from imagination to reality, cloud computing and 3D sensor technologies like Microsoft’s Kinect are being integrated into robotics. Such commercially available technologies are amongst the emerging trends in robotics as listed by both the panelists from IEEE Spectrum and Robotics Business Review.

Our features take a look at promising technologies for stroke rehabilitation and how it has impacted both caregivers and patients themselves. As you may know, when it comes to stroke rehabilitation, it takes a dedicated team to help a person regain as much independence as possible — from doctors to physiotherapists and caregivers — with the goal of providing a conducive environment for the patient. We then explored how robotics can aid in diagnosis of disease through the works of researchers marry both robotics and medicine.

Sulastri Kamis
Editor
Asia Pacific Biotech News
An open-label, randomized, international, pivotal Phase III trial has commenced of BV-NSCLC-001, Bioven’s novel therapeutic vaccine for the treatment of patients with Stage IIIb or IV non-small cell lung cancer (NSCLC). BV-NSCLC-001 is a recombinant EGF with a carrier and adjuvant that targets the EGFr pathway. The trial compares BV-NSCLC-001 with standard treatment and supportive care. It will include 438 patients at 70 centers in 11 countries, including the UK, Continental Europe, India and Southeast Asia, and is open to men and women in the age range of 20 to 65 years. It is expected that interim data will be made available in the first half of 2014.

Following the dosing of the first patient in Aberdeen, the UK, a further eight patients have been dosed at a number of approved centers across Europe. Bioven is confident that it will receive approval in the near future from the Indian Government to undertake a proportion of the trial in several Indian hospitals. The study consists of patients being vaccinated with BV-NSCLC-001 prior to, during and subsequent to chemotherapy. Interim results from an ongoing Phase III Cuban trial (involving vaccination only during and subsequent to chemotherapy), have shown promise, with the overall survival rates compared to those of current best standard practice increasing from 30 to over 50 per cent at 12 months.

BV-NSCLC-001 was in-licensed from the Centre of Molecular Immunology, Cuba, and has shown encouraging results in earlier Phase II trials, where the vaccine more than doubled survival rates compared with standard treatment. Bioven also has rights to BV-NSCLC-001 in prostate cancer and other solid tumors.
The Department of Biotechnology (DBT) of the Government of India will fund a new initiative for chemical biology and molecular therapeutics in Bangalore at the Institute for Stem Cell Biology and Regenerative Medicine (inStem) in collaboration with the National Centre for Biological Sciences (NCBS), Tata Institute of Fundamental Research. Support from multiple sources including the DBT will provide approximately INR 940M (GBP 10.5M) to establish the initiative.

Researchers in the initiative will combine methods from genetics, chemistry, cell biology, biochemistry and imaging to understand the alterations in cellular systems that underlie human diseases, and identify ways to correct them using drugs. The initiative is expected to develop powerful new scientific approaches for the treatment of diseases like cancer, integrating expertise from the basic and clinical sciences in India. It will create a multidisciplinary environment for training young researchers and physicians in the translation of fundamental research to clinical application. The new initiative is the result of a collaboration that links Professors S. Ramaswamy, K. VijayRaghavan, Satyajit Mayor and colleagues at inStem and NCBS in Bangalore, with Professor Ashok Venkitaraman at the University of Cambridge in the UK. The initiative began in September 2011 when Cambridge University’s Vice-Chancellor Professor Sir Leszek Borysiewicz signed a memorandum of understanding with the inStem and NCBS. The inStem governing council is chaired by Dr. M.K. Bhan, the Secretary, Department of Biotechnology, Government of India.

Professor Ashok Venkitaraman, who is the Ursula Zoellner Professor of Cancer Research, University of Cambridge and Director, Medical Research Council Cancer Cell Unit, says: “Having originally trained and practiced as a physician in India, I am delighted that the Department of Biotechnology, Government of India will be supporting this exciting new initiative. The excellence of my colleagues in Bangalore, and the terrific research environment they have created, inspires confidence that we can work together not only to improve our fundamental understanding of the cellular abnormalities that cause human diseases like cancer but also to translate this information for the benefit of patients.”

Professor K. VijayRaghavan, Acting Director of inStem and the Director of the National Centre for Biological Sciences (NCBS) of the Tata Institute of Fundamental Research (TIFR) says: “inStem is taking a new and adventurous path of collaborative, team-driven efforts to address the most challenging of biomedical problems. The NCBS-inStem campus provides an ideal intellectual environment for this collaboration with Cambridge to succeed. Ashok Venkitaraman is a world-leader in his area and we are delighted to work with him and Sir Leszek, also a leading biomedical researcher and former head of the UK Medical Research Council. inStem is committed to the success of this joint program, approved enthusiastically by its governing council and its Chair, Dr. M. K. Bhan, Secretary, Department of Biotechnology.”

Sir Leszek pointed out that “Cambridge and the Tata Institute, of which NCBS is a part, have a long history of connections. TIFR’s founder Homi Bhabha studied and worked in Cambridge as have many NCBS and inStem faculty. We view this very important collaboration as mutually beneficial and an example of how the best in basic research can address important biomedical questions.”
Asia–Pacific Analysis: The slow road to green energy

More Asia–Pacific countries need to embrace renewable energy and follow the first tentative steps of some governments, says Crispin Maslog.

The South-East Asia and Pacific region is blessed with abundant sources of ‘green’ energy — including sun, wind, water, biomass and geothermal — but governments are still not doing enough to harness them.

The 30 countries in this part of the world are sitting just a few degrees below and above the equator, and enjoy an estimated 300 days of sunshine a year. Advances in photovoltaic (PV) technology mean that solar energy can be harnessed even on cloudy days during the rainy season.

There are signs that renewable energy, particularly solar, is slowly being promoted in the region. Indonesia, Malaysia, the Philippines and Thailand are among countries leading the way.

These South-East Asian countries have adopted the necessary policies to attract domestic and international investment in renewable energy. Government-led initiatives include ‘feed-in tariffs’, which provide payments to small-scale green energy producers; customs and duty exemptions for energy companies; and guaranteed access to the electricity grid.

Thailand is the first country to encourage investment in large-scale solar power parks. It has just completed the Solarta 3MW Sai Sena Solar Park in Ayutthaya, 70km north of Bangkok, a model project for the region.

The park produces 4,471 megawatt hours of clean energy each year — enough to power 1,530 homes. Thailand is aiming for renewable energy to contribute a quarter of the country’s total energy mix by 2022.

Malaysia jumped on the solar energy bandwagon by introducing nonfinancial support mechanisms such as standardizing contracts between electricity providers and buyers (power purchase agreements), and by investing in infrastructure to provide grid access.

Malaysia has set a target for 2,080 megawatts or 11 percent of all electricity generated in 2020 to come from solar and other renewable sources.

Indonesia, on the other hand, has taken a slightly different route. There, the government announced last year that it is directly investing in solar energy by building communal solar power plants on 100 small islands across the country, to be followed by 1,000 more on other islands the following years. The plants will channel electricity to households in poor areas nearby.

The islands project will cost the government 900 billion Indonesian rupiah (around US$94 million) and will be implemented by Indonesia’s national electricity utility PT PLN. In addition to the island programs, PT PLN has announced that it will provide 340,000 rural households in eastern Indonesia with small solar systems, which represents a total investment of around US$139 million.

Government initiatives are at the forefront of renewable energy provision in the Philippines too. In 2008, the country launched a National Renewable Energy Program (NREP) which aims to increase the country’s renewable energy capacity — including solar energy — from 5,400 megawatts to 15,300 megawatts in 2030.

Most of the solar energy projects now operating in the country are in remote rural areas — for example, the Alliance for Mindanao Off-grid Renewable Energy Program (Amore) has been providing electricity to off-grid towns since 2002, using renewable energy sources such as solar and small-scale hydropower.

Amore is also contributing towards the government’s goal of achieving 90 per cent household electrification by 2017. To date, it has energized more than 12,000 households in 400 of Mindanao’s 13,000 barangays (villages).

The solar energy movement is also taking hold in the Pacific islands, particularly Papua New Guinea and Palau, through the Pacific Islands Renewable Energy Project (PIREP) and the Pacific Islands Greenhouse Gas Abatement through Renewable Energy Project (PIGGAREP), which promote the commercialization of renewable energy technologies.

Even though the renewable energy industry has reduced its costs by between 15 and 20% every year on average over the past ten years, renewable energy remains more expensive than building a fossil-fuelled power plant.

This is a major barrier for promoting green energy, and investment is lagging in some countries in the region. Vietnam, for example, has huge renewable energy resources, but has not yet taken advantage of this potential because of the huge funds required to construct infrastructure such as solar parks and power grids.

Solar power projects in the country therefore depend on foreign investment, meaning that solar technology tends to be restricted to state agencies and institutions.

To encourage investment into the solar power business, governments have to ensure favourable conditions for private entrepreneurs — for example, by mandating utilities to buy power generated from renewable energy sources for a certain period, during which the cost of electricity is fixed.

Other incentives include tax exemptions, duty cuts, investment grants, soft loans, government co-investment schemes and funding for research.

It is time to embrace the sun. These solar and other renewable energy projects are the way countries in South-East Asia and the Pacific must go as they face the prospect of more extreme and frequent storms and droughts associated with climate change.

Source: SciDev.net
SINGAPORE

Takeda progressing well in Asia with New Drug Applications

Seven NDAs filed within eight months in 2012 in several countries/territories. Takeda Global Research and Development (Asia) Pte Ltd (TGRD Asia), a wholly owned subsidiary of Takeda Pharmaceutical Company Limited (Takeda) announced that it is progressing well with New Drug Applications (NDA) in the Asian region. Within the first eight months of this year, seven NDAs have been filed in various countries/territories. These prescription drugs include:

- azilsartan medoxomil (development code: TAK-491) for hypertension in Hong Kong SAR
- azilsartan medoxomil with chlorthalidone (development code: TAK-491+CLD) for hypertension in Taiwan, Thailand and Indonesia
- alogliptin (development code: SYR-322) for type 2 diabetes in Australia, Mainland China and South Korea

Typically, NDA approvals take about 12 to 18 months to be approved by health regulatory bodies depending on the respective countries/territories.

Dr. James Garner, general manager for TGRD Asia said, “Patients are central to our focus and we strive towards better health for patients through leading innovation in medicine. We are very pleased with our progress in Asia as this region forms an important part of Takeda’s plans. Over the past three years, we have quadrupled the proportion of clinical trial subjects we recruit in Asia and we are actively conducting clinical trials in several countries/territories, including Australia, Mainland China, Hong Kong SAR, India, Malaysia, New Zealand, the Philippines, South Korea, Taiwan and Thailand. In the meantime, we are working closely with regulatory agencies and with our local affiliates in each country to ensure that new medicines are made available to physicians and patients in Asia as rapidly as possible.”

In China, TGRD Asia works closely with Takeda Shanghai Development Center (TSDC) to conduct Takeda’s clinical development activities within the Asian region. TSDC has a focus on China for non-oncology, and across Asia for oncology with Millennium: The Takeda Oncology Company.

TAK-491 (azilsartan medoxomil) is for the treatment of hypertension, or high blood pressure, in adults. Already approved in the United States and the European Union, it is an angiotensin II receptor blocker (ARB) that lowers blood pressure by blocking the action of angiotensin II, a vasopressor hormone that constricts blood vessels. When the angiotensin II receptor is blocked, blood vessels stay relaxed and open and blood pressure can be reduced. TAK-491 is a once-daily oral therapy for use alone and in combination with other antihypertensive medications.

TAK-491+CLD is also for the treatment of hypertension to lower blood pressure in adults. Already approved in the United States, TAK-491+CLD combines azilsartan medoxomil (TAK-491) with the diuretic chlorthalidone in a once-daily, single tablet. Chlorthalidone reduces the amount of salt and water in the body by increasing the flow of urine, which helps lower blood pressure. Lowering blood pressure reduces the risk of fatal and nonfatal cardiovascular events, primarily strokes and heart attacks. Results of a 12-week, head-to-head, Phase III study published online in the American Heart Association journal Hypertension found systolic blood pressure (SBP) reductions of a fixed-dose combination of azilsartan medoxomil and chlorthalidone 40/25 mg were statistically superior to those of the fixed-dose combination of olmesartan medoxomil-hydrochlorothiazide 40/25 mg. It is the first and only hypertension medication to combine an angiotensin II receptor blocker (ARB) with chlorthalidone, a diuretic, in a once-daily, single tablet.

SYR-322 is used for the treatment of type 2 diabetes. It is a dipeptidyl peptidase-IV (DPP-4) inhibitor, used as an adjunct to diet and exercise. It exhibits extremely high selectivity for DPP-4 inhibition and a once-daily dosing provides the benefit of convenience. It is designed to slow the inactivation of incretin hormones GLP-1 (glucagon-like peptide-1) and GIP (glucose-dependent insulinotropic peptide), which play roles in regulating blood glucose levels. As for indications, it is the only DPP-4 inhibitor that currently permits combination with alpha-glucosidase inhibitors, which are in common use in Japan, China and the Philippines.
The universities– both ranked among the top four in the world in 2012 QS Top 50 ranking of young universities under 50 years old – have jointly funded two appointments to the new Warwick-NTU Neuroscience Research@Singapore program and will hold their first annual symposium at Warwick.

The collaboration will allow Warwick to tap into the research powerhouse of Singapore’s world-renowned Biopolis biomedicine hub and the critical mass forming in neuroscience research in the country.

Dr Ayumu Tashiro and Dr Albert Chen have been taken on as the first professors to the Warwick-NTU joint program based at Biopolis.

A joint PhD in neuroscience is also currently being developed by the two institutions.

In addition a small research team will be formed with a post-doctoral research fellow being assigned to each of the two new academics, and graduate studentships will be made available.

The two professors, who hold a joint-appointment with the two universities, will be teaching undergraduate and post graduate students at NTU. Students from Warwick are set to benefit from the program through two-way visits and exchanges of materials.

Professor Tim Jones, University of Warwick Pro Vice-Chancellor: Research (Science and Medicine), Knowledge Transfer and Business Engagement, said: “Both the University of Warwick and NTU are ambitious, globally-connected universities with a strong track record in neuroscience research.

“Neuroscience at Warwick is one of our strategic priorities and has undergone significant investment and expansion in recent years.

“This link up with NTU offers significant opportunities to accelerate our activities in this area.”

Professor Stephen Smith, NTU’s Vice President (Research) said: “It is an opportune time for NTU to tie up with Warwick for neuroscience research as Singapore pushes towards research in the biomedical science industry.

“With NTU’s focus on interdisciplinary research and with our new medical school starting next year, I believe the joint-research effort will see synergistic collaborations between our institutions, yielding important research insights into the workings of the brain and eventually, enabling scientists and doctors to develop new treatment and biomedical tools.”

Scientists at Biopolis are working on optogenetic tools – genetically-encoded light-activated ion channels and pumps used to map neural circuitry.

The new Warwick-NTU partnership aims to build a complementary strand of research in this area for use in investigating how the brain develops specific synaptic connections between neurons, how neural stem cells in the adult brain contribute to plasticity of neural circuitry; and how the brain creates spatial maps to memorize locations.

The program will take place in laboratories provided to it by the Agency for Science, Technology and Research (A*STAR), Singapore’s government agency dedicated to supporting science, technology and research.

The partnership will also enable both partners to participate in the expanding Neuroscience Research Partnership in Singapore, a collaboration between A*STAR and Duke-NUS Graduate Medical School.

“Both the University of Warwick and NTU are ambitious, globally-connected universities with a strong track record in neuroscience research” — Professor Tim Jones
Ms. Monsanto Thailand Ltd. organized the Monsanto’s Beachell–Borlaug International Scholarship (MBBIS) Certificate Ceremony at Siam Kempinski Hotel, Bangkok to announce the first Thai to be awarded the Scholarship in 2012.

Mr. Eakpol Phuvanartnarubal, a graduate student of Kasetsart University, was selected for this prestigious award. He will be conducting a research titled “Breeding-by-design: New Submergence Tolerance Rice Prolong Flash Flooding Environment” with a main goal to improve rice variety with tolerance to prolonged flooding, a trait that is likely to be in demand both locally and internationally. The project will be supervised by Assoc. Prof. Apichart Vanavichit, Director of Rice Gene Discovery Unit, which was established through the close collaboration between BIOTEC and Kasetsart University.

Mr. Eakpol Phuvanartnarubal will be conducting a research titled “Breeding-by-design: New Submergence Tolerance Rice Prolong Flash Flooding Environment”.

The MBBIS program was established in 2009 in honour of two of the world’s most pre-eminent rice and wheat breeders, Drs. Henry Beachell and Norman Borlaug, with a prime objective to develop highly educated rice and wheat plant breeders who can serve as future agricultural leaders. The Program is open to students worldwide who are seeking a Ph.D. in rice or wheat improvement through plant breeding.
Open access will change the world, if scientists want it to

While the Australian Research Council considers its policy on open-access publication and others within the scientific community call for the increased sharing of scientific data, the British are already a step ahead.

They are implementing plans to make all publicly funded scientific research available to anyone by 2014 – for free. This signals a dramatic change for British universities and academics whose current scientific research is only available through expensive subscription-based journals.

But as we edge closer to open-access publishing, there has been much hand-wringing among the scientific community.

The dilemma is this: all scientists want to publish in high-impact journals but we also want our work accessible to as wide an audience as possible. In other words we want the prestige, but we also want the popularization of our work that open-access publication can bring.

But for scientists in developing countries, the open access movement could mean the world.

So what is the issue? Basically, scientists who work for public-funded institutions rely on the global tax-payer to underwrite much of what we do. And so, you would think, what we produce should then be made public for the global public good.

But as a scientist, the “publish or perish” mantra is taken very seriously. Failure to do so represents not only a shortfall of professional responsibility to account for the funds made available for our research, but individual careers are often made (or broken) on one’s publication record.

Unfortunately, many of the journals in which we publish are owned by large publishing houses that control access to scientific information. This is primarily through the levy of subscription fees and these are increasing.

Between 1986 and 2002 overall subscription rates increased by 227%, making most journals prohibitively expensive to all but the better-resourced institutions. Such high fees also contribute to the vast profits of the publishers. The Economist recently reported that publishing house Elsevier alone made a profit of US$1.2 billion in 2011.

Essentially, subscription journals privatize the public investment of science – a process scientists contribute to through the voluntary peer-review process.

If you are able to pay subscription costs, as most northern institutions are, then it is relatively easy to keep abreast of new scientific developments. But if you are a developing-country scientist from a government research organization or university that cannot afford subscription fees, the likelihood is that you won’t be able to access the latest science.

Inevitably, you will get left behind.

This precipitates a cycle in which well-resourced colleagues dominate the scientific literature. In rank order, the United States, the United Kingdom, Germany, Japan, France, Canada, Italy and Switzerland produce 85% of the world’s most cited publications.

But this trend is changing.

The fact the Guardian and the Economist, two of the UK’s most respected media outlets, are covering the issue of open-access publishing is indicative of the fact it’s an important subject, worthy of discussion.

At the time of writing, more than 11,000 scientists have signed up to a boycott of Elsevier which controls a major share of the market.

In an incredible act of altruism, or as he describes it, a possible “toxic career move”, Winston Hide of the Harvard School of Public Health recently resigned as Associate Editor of the journal Geonomics in protest against:

... a system that provides solid profits for the publisher while effectively denying colleagues in developing countries access to research findings.

Open-access publishing is now being advocated by many institutions. Even such a well-endowed entity such as Harvard University is encouraging its scientists to focus on open-access publishing both for ethical reasons and the fact that subscribing to what is essentially private journals is “fiscally unsustainable”.

The Wellcome Foundation, which funds a great deal of medical research, has insisted much of the findings resulting from its portfolio are published in open-access journals. It is expected that many other institutions and foundations will follow such examples.

My own institution, the Centre for International Forestry Research, will soon be undertaking a review of the costs and benefits of open-access versus subscription journal publication, an issue that myself and colleagues discussed not so long ago (admittedly in a subscription journal!)

For scientists, the debate represents a considerable dilemma. The historical model of scientific dissemination, and our own career paths, still promotes publishing our work in “exclusive” high-impact journals.

But open-access publishing can increase one’s citation index considerably – something all scientists pay considerable heed to – often by up to 127%.

More and more open-access journals are seeing their impact factor increase significantly (see, for example, PloS, PNAS). This is only achieved by scientists being willing to submit high-quality research papers to such journals.

The more this happens, the more open-access journals are being seen as credible and prestigious. And in terms of popularity, open-access publishing makes our research available to anyone with an internet connection.

Who wouldn’t want that?

Terry Sunderland
Source: The Conversation
Verisante places Aura Beta Units for safety, verification testing in B.C., Alberta and Ontario clinics

Verisante Technology, Inc., a leader in cancer detection technology, announced that Aura™ Beta units continue to be placed at field testing sites across Canada.

Aura™ is indicated for use for the evaluation of skin lesions that may be clinically suspicious for melanoma, squamous cell carcinoma and/or basal cell carcinoma when a medical professional chooses to obtain additional information to rule out one of the above conditions before making a final decision to biopsy.

After initial testing at the Skin Care Centre at Vancouver General Hospital (VGH) and at the BC Cancer Agency, beta units have been placed in Calgary and Edmonton, with additional units to be placed in Ontario for tests on consenting patients.

“Testing our beta units in real world conditions is an important final step as we ready to make the device available in the markets where we have approval to sell, and move towards full commercialization of Aura™,” said Thomas Braun, President & CEO. “Aura™ is a proven device, which has the potential to improve patient outcomes, reduce wait times and also save the health care system time and money.”

Field testing is expected to last three to four months, during which both patients and clinicians are blinded to Aura™ results. The purpose of the testing is to refine usability, assess how it works in a clinical environment and to collect data that will be used for software verification purposes.

“As a practicing dermatologist, I see the growing need for a device such as Aura™ to better serve our patients,” said Dr. Andrei Metelitsa, co-director, Institute for Skin Advancement, and clinical assistant professor, Division of Dermatology, University of Calgary. “Clinical study results show the ability of Aura™ to efficiently assist in diagnosing skin cancer. Any tool that can be used to evaluate suspicious skin lesions quickly and accurately is a welcome addition to a dermatological practice.”

As part of the University of British Columbia’s clinical study, the Verisante Aura™ was used to scan approximately 1,000 lesions at the Skin Care Centre at VGH over a six-year period. Results from that study published this year in Cancer Research, a peer-reviewed journal of the American Association of Cancer Research, showed the Verisante Aura is 99% accurate in differentiating all major skin cancers from benign lesions and the device offers the potential for reducing unnecessary biopsies by 50 to 100%.

Aura™ is a non-invasive optical system that uses Raman spectroscopy to biochemically analyze the skin, providing immediate and accurate results. The device will help to automate the current process of diagnosis, allowing rapid scanning of the 20 to 40 skin lesions on at-risk individuals, improving patient outcomes and comfort.

Early detection is key to saving the lives of melanoma patients and saving healthcare costs. When melanoma is diagnosed and treated in the earliest stages, the survival rate is 99% and it costs about $1,800 to treat it. In the late stages, the survival rate decreases to 15%, while the cost to treat it increases to $170,000.
Life Technologies sets new worldwide standard for criminal forensic testing with introduction of GlobalFiler™ Express Kit

Life Technologies Corporation, the world’s leader in human identification solutions, launched the GlobalFiler™ Express kit, a new DNA kit that will revolutionize how crime labs perform forensic testing around the world -- making it faster, easier and cheaper to process DNA samples.

By increasing the number of genetic markers by over 30% to 24, GlobalFiler™ Express delivers the ability to recover significantly more information from forensic samples and increases discrimination power by up to 9 orders of magnitude. This results in faster and more powerful comparisons of forensic data to resolve crimes. Combined with five times faster processing efficiency, this powerful advancement will enable forensic scientists to solve and prevent more crime while addressing ever-growing backlogs. To date, 44 countries have now implemented criminal offender DNA database programs with a combined offender sample pool of 40 million and growing.

"I’ve been very impressed with GlobalFiler's performance," said Professor Walther Parson, Ph.D., a leading world expert in forensic DNA testing in Innsbruck, Austria. "It's extremely high discrimination power will greatly facilitate intelligence databasing and solving of national and cross-border crime."

The GlobalFiler™ kit portfolio which includes the GlobalFiler™ Express kit for reference sample processing and the GlobalFiler™ kit for casework evidence, features a new, proprietary chemistry that enables 48 samples to be processed in under two hours when combined with Life Technologies’ forensic testing systems -- five times faster than other solutions currently on the market. It also facilitates quicker and improved amplification of challenging samples, such as degraded human remains. All combined, the new kits offer forensic science customers an unsurpassed standard in rapid DNA processing from sample-to-result.

For more than 25 years, Life Technologies has led the development and commercialization of the industry's most trusted and reliable forensic solutions for human identification (HID) testing. It is also the only company in the world that designs and validates its reagents, instruments and data analysis software together as an integrated system for HID testing.

"No other company understands the needs of forensic scientists better than we do and as a result, we have delivered a product that will dramatically change the way forensic testing is done on a global scale," said John Gerace, Head of Applied Sciences for Life Technologies. "We know that time and costs are of critical importance when it comes to solving crimes."
How immune cells can nudge nerves to regrow

A technique to alter cells that respond to injury dramatically increases the rate of nerve repair, according to an animal study.

If the results can be applied to humans, the method could one day lead to a new strategy for treating peripheral nerve injuries, such as those that typically result from trauma.

“Both scar formation and healing are the end results of two different cascades of biological processes that result from injuries,” says Ravi Bellamkonda, a professor of biomedical engineering and member of the Regenerative Engineering and Medicine Center at Georgia Tech and Emory University.

“In this study, we show that by manipulating the immune system soon after injury, we can bias the system toward healing, and stimulate the natural repair mechanisms of the body.”

Beyond nerves, researchers believe their technique could also be applied to help regenerate other tissue—such as bone. The research is reported in the journal Biomaterials.

After injury, macrophage cells that congregate at the site of the injury operate like the conductor of an orchestra, controlling processes that remove damaged tissue, set the stage for repair and encourage the replacement of cells and matrix materials, says Nassir Mokarram, a PhD student at Georgia Tech.

Converting the macrophages to a “pro-healing” phenotype that secretes healing compounds signals a broad range of other processes—the “players” in the symphony analogy.

“If you really want to change the symphony's activity from generating scarring to regeneration of tissue, you need to target the conductor, not just a few of the players, and we think macrophages are capable of being conductors of the healing symphony,” explains Mokarram.

Macrophages are best known for their role in creating inflammation at the site of injuries. The macrophages and other immune system components battle infection, remove dead tissue—and often create scarring that prevents nerve regeneration. However, these macrophages can exist in several different phenotypes depending on the signals they receive. Among the macrophage phenotypes are two classes that encourage healing: M2a and M2c.

Bellamkonda’s research team used an interleukin 4 (IL-4) cytokine to convert macrophages within the animal model to the “pro-healing” phenotypes.

They placed a gel that released IL-4 into hollow polymeric nerve guides that connected the ends of severed animal sciatic nerves that had to grow across a 15 millimeter gap to regenerate.

The IL-4 remained in the nerve guides for 24 hours or less, and had no direct influence on the growth of nerve tissue in this short period of time.

Three weeks after the injury, the nerve guides that released IL-4 were almost completely filled with re-grown axons. The treated nerve guides had approximately 20 times more nerve regeneration than the control channels, which had no IL-4-treated macrophages.

Research is now under way to develop the technique for determining how soon after injury the macrophages should be treated, and what concentration of IL-4 would be most effective.

“We believe immune cells are the ‘master knobs’ that modulate the biochemical cascade downstream,” Mokarram says. “They are among the ‘first-responders’ to injury, and are involved for almost the whole regeneration process, secreting several factors that affect other cells. With IL-4, we are doing something very early in the process that is triggering a cascade of events whose effects last longer.”

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As part of their paper, the researchers defined a state they termed “regenerative bias” that predicts the probability of a regenerative outcome. The Bellamkonda group discovered that when it quantified the ratio of healing macrophages to scar-promoting macrophages at the site of injury early after the injury, the ratio—or regenerative bias—predicted whether or not the nerve regenerated after many weeks.

“The significance of this finding is that IL-4 and other factors may be used to make sure the regenerative bias is high so that nerves, and perhaps other tissues, can regenerate on their own after injury,” Bellamkonda says.

Source: Futurity.org
A combined team of University of Minnesota biomedical engineers and researchers from Mayo Clinic have released data from a "groundbreaking" study concerning a new type of non-invasive brain scan taken immediately after a seizure gives additional insight into possible causes and treatments for epilepsy patients. The findings could specifically benefit millions of people who are unable to control their epilepsy with medication.

In the trial, researchers studied the brains of 28 patients immediately after seizures, or what is technically known as the "postictal" phase of a seizure. They used a specialized type of non-invasive EEG with 76 electrodes attached to the scalp for gathering data in contrast to most previous research that used 32 electrodes. The researchers used specialized imaging technology to gather data about the patient. The findings may lead to a way of locating the brain regions responsible for seizures in individual patients using non-invasive strategies.

The study uncovered data about brain function that can be gathered through non-invasive methods, not only during a seizure, but immediately after a seizure. The frontal lobe of the brain was found to be most involved in severe seizures.

Additionally, seizures in the temporal lobe were found to be most common among adults. The technique used in the study could also help determine the side of the brain where the seizures originate.

Describing the study as "a paradigm shift for research in epilepsy", Bin He, a biomedical engineering professor in U-M’s College of Science and Engineering and senior author of the study, says the research is also the first where new non-invasive methods were used to study patients. Epilepsy affects nearly three million people in the US and 50 million people worldwide. The biggest challenge for medical researchers has been to locate the part of the brain responsible for the seizures to determine possible treatments. In the past, most research has focused on studying patients while they were having a seizure, or what is technically known as the "ictal" phase of a seizure. Some of these studies involved invasive methods such as surgery to collect data.
EYE ON CHINA

Institute of Biological Chemistry researchers find new protein–DNA interaction

A recent study by a research team from the Institute of Biological Chemistry (IBC) led by Distinguished Research Fellow Andrew H.-J. Wang has increased understanding of the molecular mechanism of antibiotic resistance in the Staphylococci bacteria. The team found that multiple antibiotic resistance regulator TcaR in Staphylococcus epidermidis can bind to single-stranded DNA (ssDNA) and inhibit its replication. It is hoped that the findings, published online in the scholarly journal PLoS One, will aid the development of new treatments for Staphylococci infection.

The Staphylococci bacteria are one of the most common causes of bacterial infection. They can cause a wide variety of diseases in humans through invasion and toxin production, and also by producing biofilm to protect themselves from the host immune system and the action of antibiotics. Staphylococcus aureus is the most well-known species as it the cause of many antibiotic resistant hospital– and community-acquired infections. The protein TcaR from the multiple antibiotic resistance repressor (MarR) family of proteins is known to be responsible for the regulation of antibiotic resistance and biofilm formation in Staphylococci; however, the detailed mechanism of its action is unknown.

In the study, the team used electrophoretic mobility shift assay (EMSA), circular dichroism (CD), and Biacore analyses to show that the TcaR protein can interact strongly and cooperatively with ssDNA, thereby identifying a new role for MarR family proteins. In order to investigate the regulation mechanism of the ssDNA binding ability of TcaR, the team further used electron microscopy to reveal the TcaR-ssDNA complex. Their study also showed that TcaR could inhibit viral ssDNA replication and provide viral resistance against ssDNA phage in E. coli. Overall, the study suggests that TcaR plays of role in regulation of DNA replication.

The MarR family proteins are involved in multiple antibiotic resistances. They are sensors of changing environments, allowing pathogenic bacteria to survive and persist in a dynamic environment. Up to now, the knowledge of MarR family protein-nucleic acid interaction has been limited to double-strand DNA (dsDNA); this is the first study showing that MarR family proteins also interact with ssDNA.

"It is very exciting that we present the first attempt to investigate the TcaR-ssDNA interaction. We anticipate that the results of this work will extend our understanding of MarR family proteins and broaden the development of new therapeutic strategies for Staphylococci," said Distinguished Research Fellow Wang.

The research was conducted and financed by Academia Sinica and grants from the National Research Program for Biopharmaceuticals, a project funded by the National Science Council of Taiwan.

Source: Wikimedia Commons
Medicago to receive up to US$12 million

Medicago Inc., a biopharmaceutical company focused on developing highly effective and competitive vaccines based on proprietary manufacturing technologies and Virus-Like Particles (VLPs), announced the signing of a licensing agreement with Philip Morris Products SA (PMP), a subsidiary of Philip Morris International Inc., an international tobacco company with products sold in approximately 180 countries. Under the agreement, Medicago grants PMP an exclusive license to develop, commercialize and manufacture Medicago’s pandemic and seasonal influenza vaccines for China. In addition, Medicago has signed an exclusive, worldwide license for a portfolio of plant-based protein development technologies from PMP. Medicago will receive an upfront payment of US$4.5 million from PMP. In addition, Medicago is eligible to receive development milestone payments totaling US$7.5 million, as well as royalty payments on any future sales of pandemic and seasonal influenza vaccines by PMP in China which utilize the Medicago technologies.

In a separate agreement, in exchange for signing an exclusive, worldwide licensing agreement, Medicago has licensed a portfolio of plant-based protein development technologies from PMP. These technologies include tools and methods for producing proteins in plants which are expected to complement Medicago’s existing patent portfolio. Medicago will pay US$0.7 million to PMP, and there are no additional milestone payments associated with this agreement. PMP is entitled to receive royalty payments on any future sales of Medicago products which utilize the technologies licensed from PMP.

“We look forward to working closely with PMP to develop our pandemic and seasonal influenza vaccine candidates in the coming years,” said Andy Sheldon, Chief Executive Officer of Medicago. “Strengthening our VLP platform and international expansion to emerging markets like China is a key component of our growth strategy, and this partnership represents an important milestone in achieving this strategy.”

Medicago’s pipeline includes the initiation of a U.S. Phase IIa clinical trial for a quadrivalent seasonal flu vaccine, with interim data expected in the first quarter of 2013. A Phase I clinical trial for a H5N1 VLP vaccine with a new adjuvant is planned in partnership with the Infectious Disease Research Institute (IDRI), with interim data expected in the first quarter of 2013. GMP process development and a GLP toxicology study for a rabies vaccine are ongoing. Medicago is also working with Mitsubishi Tanabe Pharma under a strategic alliance to develop a vaccine for rotavirus, and at least two additional vaccine candidates. In addition to vaccines, Medicago is conducting research and development in the area of biosimilar products.
INEX inks partnership with BGI for new non-invasive prenatal test

INEX Innovations Exchange Pte. Ltd., a women’s health diagnostics company based in Singapore, announced its partnership with BGI, the world’s largest genomic sequencing institute and bioinformatics powerhouse, to establish a Next Generation Sequencing facility in Singapore to offer a suite of molecular genetics tests, starting with iGeneScreen™, a non-invasive prenatal test to detect fetal chromosomal abnormalities in pregnant women.

Developed by researchers at BGI using a modern genomic sequencing technology called Next Generation Sequencing (NGS), iGeneScreen™ is a blood test that analyzes fetal DNA in maternal blood to detect chromosomal abnormalities. It is a non-invasive screening test requiring only a 5ml blood sample from pregnant women at 12 weeks or later, and it provides highly accurate prenatal test results for Trisomy 13 (Patau Syndrome), Trisomy 18 (Edwards Syndrome) and Trisomy 21 (Down Syndrome).

Amniocentesis is currently the most common invasive prenatal diagnosis procedure offered to pregnant women at increased risk of Down Syndrome, and it carries a 1% risk of miscarriage. The new test will provide a safer alternative for pregnant women at risk of having babies with chromosomal abnormalities.

“We are extremely excited at the prospect of embarking on this relationship with BGI. It is a mutually beneficial partnership in that they will provide the molecular genomic facility and a wealth of sequencing and bioinformatics expertise, and we will offer the technical infrastructure, regional knowledge and distribution network”, said Dr. Sidney Yee, Executive Director at INEX.

“Singapore will be the only facility in Asia outside of China offering such a test. This entity is poised to be a Centre-of-Excellence facility that receives and processes tests from South and South-East Asia, the Middle East and Australasia. This first trimester non-invasive prenatal test has huge advantages in that it is highly accurate with a sensitivity of over 99%, and an extremely low false positive rate of below 1%. All this while posing absolutely no risk to the fetus, so we are confident that it will be well received by all pregnant women,” she continued.

Regarding this exciting partnership in Singapore, BGI’s Chief Operating Officer, Dr. Yin Ye, commented, “BGI is delighted to partner with INEX to jointly establish the Next Generation Sequencing facility in Singapore. BGI, the largest sequencing institute in the world, is offering this non-invasive prenatal test (NIPT) with breakthroughs in bioinformatics analysis. To-date, we have performed over 60,000 such NIPT tests.”

“This new state-of-the-art facility here in Singapore is an important next step for BGI, as Singapore is renowned for its robust regulatory framework, highly-skilled molecular technologists, and its excellent reputation for translational research and medical diagnostics. Furthermore, INEX’s long experience and research innovation in molecular diagnostics makes it a natural choice for us to partner with here in Singapore. With this facility here in Singapore, and working closely with INEX, we are looking forward to expanding our influence and offerings within the sphere of medical genomics and medical diagnostics in the Asia-Pacific region”, he continued.

The facility in Singapore is expected to be operational by the first quarter of 2013.
China emerging as 'major player' for pharmaceuticals

China wants to become a major developer of vaccines for the developing world. The pharmaceuticals industry is starting to take much more notice of China, as the country emerges as a major developer of vaccines for the developing world.

China’s drugs industry is close to being given the go ahead to manufacture the Japanese encephalitis vaccine for the developing world.

According to the British Medical Journal, this will mark it out as a “major new player” in the market.

Seth Berkley, chief executive of the GAVI Alliance, believes that Chinese drugs firms will be ready by the start of next year for the World Health Organization (WHO) to carry out pre-qualifications inspections of production of the vaccine.

There has been a push for contract services with Asia in recent times, thanks to the region’s growing presence in the pharmaceutical market.

China’s rise is likely to further facilitate the establishment of outsourcing agreements between the west and Asia, once it has the processes in place to develop such vaccines on a mass scale to WHO requirements.

Once the WHO checks have been carried out, the United Nations will be able to purchase the vaccine for countries without their own regulatory systems.

Possible cure for dementia found by Taiwan researchers

A southern Taiwan-based National Cheng Kung University (NCKU) research team has discovered that rapamycin, a drug as a autophagy activator is a possible treatment to alleviating frontotemporal lobar degeneration (FTLD), one of the mainly causes of dementia, and so far no medication can be used.

The medical breakthrough made by the team led by Kuen-Jer Tsai, professor of the Institute of Clinical Medicine and Institute of Basic Medical Science, NCKU, was published in Proceedings of the National Academy of Sciences of the United States of America, PNAS.

To activate autophagy, the process of self-digestion by a cell, is the crucial discovery of the research, according to Tsai adding that autophagy activators rescue and alleviate pathogenesis of a mouse model with protein pathies of the TAR DNA-binding protein 43 (TDP-43), a neuronal activity, which is the main syndrome of FTLD.

“The pathological and clinical syndrome of FTLD including the brain atrophy of frontal and temporal lobe, memory loss, speechless, neuromotor disorders, even would be complicating with motor neuron disease,” said Kuen-Jer Tsai.

In the elderly population over the age of 65, FTLD is the fourth most common reasons of dementia, only after Alzheimer’s disease, Lewy body dementia and vascular dementia.

However, FTLD is the second common reason of dementia just next to Alzheimer’s disease in the population less than 65 years old, according to the team.

Recent studies have found the mis-metabolism of a protein, which can affect TDP-43, is correlated to several neurodegenerative diseases, including FTLD and amyotrophic lateral sclerosis, ALS.

In the earlier stage, Kuen-Jer Tsai’s team had transgenically overexpressed TDP-43 in the forebrain of a mouse, successfully developing an animal model existing phenotypic characteristics mimicking of FTLD.

Tsai’s team applied the animal models with an autophagy activator in the early stage of pathology, discovering that it not only maintains the learning/memory ability of the animal model but also slows down the loss the motor function, and reducing cytosolic overexpression TDP-43 and its abnormally aggregation, therefore ameliorating the proteinopathy-induced neuronal apoptosis.

Delivering the autophagy activators at the late stage of disease progression can ameliorate the motor function, according to Tsai.

The team has also showed that spermidine, carbamazepine, and tamoxifen are autophagy activators like rapamycin could also be used to the treatment of FTLD.
The Children's Hospital of Philadelphia (CHOP) and BGI announced that the BGI@CHOP Joint Genome Center will begin to offer clinical next-generation sequencing (NGS) services at CHOP through the hospital's Department of Pathology and Laboratory Medicine in a CAP/CLIA-compliant environment.

The Clinical Laboratories Improvement Act of 1988 (CLIA) established quality standards for all laboratory testing to ensure the accuracy, reliability and timeliness of patient test results regardless of where the test was performed. The College of American Pathologists (CAP) Laboratory Accreditation Program is widely recognized as the “gold standard,” since it meets or exceeds CLIA requirements and serves as a model for various federal, state, and private laboratory accreditation programs throughout the world.

Supported by CHOP’s and BGI’s excellent infrastructure and extensive experiences in NGS services, the BGI@CHOP Joint Genome Center was established in November 2011 under the partnership between CHOP and BGI to focus on discovery of genes underpinning rare and common pediatric diseases using next-generation sequencing.

Robert W. Doms, pathologist-in-chief and chair of Pathology and Laboratory Medicine at CHOP, said, “The BGI@CHOP Joint Genome Center, operating under the umbrella of the CAP-certified Molecular Genetics Lab at CHOP, plans to launch clinical exome sequencing in the near future.”

Catherine Stolle, director of CHOP’s Molecular Genetics Laboratory, added, “This CAP-compliant NGS facility will enable us to rapidly expand into clinical NGS tests for diagnosis of specific diseases including heritable disorders and pediatric cancer.”

“BGI has been offering NGS and NGS data analysis services in a research setting since 2007,” Dr. Jun Wang, Executive Director of BGI, said in a statement. “By working together with the CHOP Pathology Department, we will be able to leverage our NGS expertise to help clinicians better diagnose and treat their patients. BGI will also be able to extend our services to support new drug development and pharmaceutical clinical trial studies in compliance with CAP and CLIA standards.”

At present, the Joint Genome Center is equipped with 5 high-throughput sequencers with the permanent space under renovation, and plans to scale up to 20 sequencers. The center has embarked on a number of projects with CHOP researchers, including an NIH-funded research grant to explore the use of NGS in a clinical diagnostic setting (co-led by Ian Krantz, and Nancy Spinner). The Center’s service portfolio includes human whole exome sequencing, targeted sequencing, whole genome re-sequencing and specialized applications such as ChiP-Seq and RNA-Seq, and NGS data analysis.
Biologists at Academia Sinica develops a new molecular strategy to suppress Hepatitis C virus replication

A research team at Academia Sinica led by Drs. Michael M.C. Lai at the Institute of Molecular Biology and Tien-Hsien Chang at the Genomics Research Center recently uncovered a key molecular player in hepatitis C virus replication. The team found that reducing the abundance of a cell component called the “40S ribosomal subunit” in a host cell could significantly cut down hepatitis C virus replication without negatively impacting host-cell health. This finding suggests a new strategy for combating hepatitis virus infection. The study was published in the scholarly journal PLoS Pathogens.

Hepatitis C is a blood-transmitted virus that causes chronic liver diseases that threaten roughly two percent of the world’s population. So far, there is no hepatitis C vaccine and current therapies are only effective in a fraction of infected patients.

Viruses rely heavily on their host cells to replicate. Research Associate Jing-Ying Huang, the first author of the article, and her colleagues in the Institute of Molecular Biology used RNAi technology to systematically search for the components of the host cell that the hepatitis C virus must borrow to successfully reproduce itself. She singled out the 40S ribosomal subunit. The 40S ribosomal subunit is normally found in sufficient abundance to satisfy the needs of both the host cell and the virus, but when the amount of the 40S ribosomal subunit is reduced below a certain threshold, the hepatitis C virus apparently becomes the weaker competitor and dwindles to its demise. Dr. Chang made an interesting analogy of this finding: “It is like how, under favorable conditions, counterfeit cell phones may work nearly as well as the well-designed name brands in drawing signals. However, once the bandwidth of the signals falls below a certain threshold, those counterfeiters fail to work, yet the name brands remain fully functional. Sooner or later, those counterfeits will fade away from the market, i.e., they will not be able to compete effectively with the name brands”.

The finding provides a new strategy through which it becomes realizable to develop effective drugs to combat the hepatitis C virus. Conventionally, drugs have been designed to target the viral proteins, but mutations that accumulate through rapid cycles of viral replication often lead to emergence of drug-resistant viral strains. In contrast, the host cell’s ribosomal 40S subunit has been perfected over millions of years of evolution, thus is extremely unlikely to morph or mutate as freely as viruses.

“Finding a good way to fine-tune 40S ribosomal subunit level as part of an hepatitis C virus therapy may not only be feasible, but also superior in terms of minimizing the drug-resistance problem” said Dr. Lai.

Molecular cloning, characterization, and expression analysis of genes encoding Gibberellin 20–Oxidase in Dasypyrumvillosum dwarf mutant

Dwarfism in cereal crops which are grown under intensive agriculture can have a positive influence on crop agronomy by increasing lodging resistance and decreasing the chances of damage due to wind and rain. For this reason, the identification and characterization of the dwarf and semi-dwarf phenotype plants are especially important. There are various contributing factors for the expression of dwarf phenotypes in plants, and the plant hormone gibberellic acid (GA) is one of the most important determinants of plant height.

Dwarfism is often caused by mutations in genes controlling the biosynthesis or signaling pathway of GA. For example, in the 1960s, a high-yielding semi-dwarf variety of rice, IR8, was achieved by introducing a major dwarfing gene (sd-1) that encoded a defective GA 20-oxidase (GA20ox) gene, which led to the rice “green revolution”. At the same time, a dominant wheat semi-dwarf cultivar Norin 10 carrying Rht genes facilitated a burst in productivity and led to the wheat green revolution. Norin 10 contained the Rht-B1b (formerly called Rht1) and Rht-D1b (formerly called Rht2) alleles that encode a mutant form of DELLA protein, a GA signaling repressor. These studies demonstrated that controlling GA biosynthesis or signaling was crucial for the production of plants with suitable height for modern production methods.

Thirty-six gene sequences encoding the gibberellin (GA) 20-oxidase were obtained from Dasypyrumvillosum and its dwarf mutant. Sequence alignment showed that there were 21 SNPs and 4 InDels among these sequences which could be divided into three haplotypes—haplotype I, II, and III with 1,293, 1,297, and 1,294 bp in length, respectively. They contained a CDS with 1,080 bp in length encoding a putative polypeptide of 359 amino acids. Two haplotypes were found in wild type (I and II) and dwarf mutant (II and III), respectively. Q-PCR analysis showed that in the whole growing stages, the majority expression levels of haplotypes from wild types were higher than that of dwarf mutant, suggesting that wild types could synthesize more active GA substrates than dwarf mutant.

The expression level in stem nodes and internodes between wild type and dwarf mutant were not significantly different, whereas their expression levels in roots were distinctly distinguished from each other in seedling, stem elongation, and heading stages, implying that most active GAs were synthesized in the root, and some were consumed by the root itself, and the others might be transported to other organs.
Everything in your body, when injured, can be healed or repaired, except your spinal cord. Imagine the cable that connects your brain to your muscles is broken – either cut or damaged from an accident – your brain won’t be able to send through its signals to and from the muscles below the lesion thus no movement can happen, at the very least. This condition is usually permanent, as the injured spinal cord cannot be healed, at least for now. There are other complications that come along with spinal cord injury (SCI), but the most obvious are paralysis, with different degrees of sensory and movement ability.

As paralysed muscles require signals from the brain to make contractions, that ability is lost with paralysis. In the long run, the muscles will be atrophied, in other words they shrink and become weak. Thus it is important for the muscles fibres to be kept active so that it retains the mass, endurance and strength. Keeping the muscles working, especially the lower limb muscles, ensures greater physical activity can be achieved, which in turn maintains whole body blood circulation, heart fitness, and potentially the bone strength (1). The best output, even if the mentioned benefits are minimal, is having a healthy psychosocial outlook amongst the spinal injured participants, as the general comment given was “… knew your muscles actually move, which you cannot possibly...
achieve otherwise, is a great feeling by itself, let alone the fitness benefits that comes with it”.

How is this artificial signal being conveyed to the muscles? In its simplest form, not from the brain, but through an external controller via a technology known as Functional Electrical Stimulation (FES). FES-evoked exercise and other activities involving artificial stimulation of the muscles started in the 1960s when researchers started to contract and move paralysed muscles through electrical stimulation to perform standing and upright stepping. FES exercise systems are now being integrated into their rehabilitation to optimize training (2). A pair of electrode is placed on the skin surface at opposite ends of the muscle, so that when current is sent as signal, the current will flow through the muscle fibres as if it were signals from the brain. This electrical activity would evoke the actin and myosin activity of the muscles, producing real contractions which can produce force and power as normal contractions would.

However, as it is not originated from the brain, the characteristics of the signal might not be optimally similar with the natural signal and pattern our brain would send, thus the duration and smoothness of the contraction would be less than natural contractions. Well-conditioned paralyzed leg muscles that perform evoked cycling could only normally produce significant force and power for about 30 minutes at maximum allowable current of 140mA before the muscles get fatigue and no longer contracts, even with electrical stimulation. This is the main problem of electrical stimulation that hinders the achievement of its great potential benefits to SCI individuals.

Therefore, to overcome this problem, researchers have investigated the optimal electrode placement and current stimulation parameters – its frequency, amplitude, duty cycle, monophasic or biphasic current, and the like. They also studied the duration and frequency of training that would deliver optimum benefits to the SCI users. Nevertheless, the gained end benefit so far is still not significant enough for a daily activity level, as the muscles still gets fatigue very easily and quickly. Some group of researchers also performed implanted FES where the electrodes are inserted through the skin directly at the nerve or muscle fibres, to increase specificity and potentially minimize the fatigue effect. This method is more promising, with better functional outcomes such as stepping, walking and grasping.

However, some SCI users prefer to have FES as an optional treatment for muscle and body conditioning only, thus might shy away from implanted FES and are more comfortable with surface stimulation and regular series of evoked FES based training such as cycling exercise. Three main muscles of the legs, i.e. the quadriceps, hamstrings and in some studies, the gluteal are the most commonly reported to being stimulated.

Cycling based FES activity comes in a variety of nature, and has developed over the years. An indoor gym-based ergometer developed by Fornusek and colleagues of the University of Sydney, Australia allows SCI users to perform FES cycling with power performance indicator calculated in real time (3). Of outdoor nature, one example is the Berkelbike, developed in the Netherlands, which allows hand and leg cycling with built-in electrode cables for the leg muscles and encoders at the bicycle crank. Virtual reality (VR) has also been embedded into an FES-based cycling system to allow indoor activity with an “outdoorsy” feel, complete with performance indicators such as power, duration, and slope degree amongst others.

A study on VR based FES cycling amongst SCI users were jointly conducted in the University of Sydney and the University of Malaya, Malaysia. These tackle primarily the ‘motivational’ factor amongst its users amongst other reasons.

Another innovation introduced by Glen Davis and Che Fornusek is to use an isokinetic mode of cycling, where the speed of cycling is set constant (3). This enables assisted movement even though the muscles are still very weak and unable to produce movement by itself, which also allows a good range of motion exercise for the leg joints. At the same time, if the muscles are stronger and able to push hard against the foot pedals, isokinetic mode provides instantaneous resistance adaptive to the leg muscle strength, as it tries to keep the rotational speed constant at any point in time. This method of training is especially useful in low speed, or cadence, as the gain in muscle strength and muscle mass is significantly greater at speed 20 rpm and lower. Also, it is worth to note that cycling at lower speed prominently builds the muscles as compared to higher speed which contributes better to heart and lungs training.

Apart from modification and optimization of stimulation current parameters, frequency and duration of exercise, and the mode of cycling, one other dimension to add to the variable is movement pattern. We
have established that an elliptical stepping pattern, in a seated body position suitable for SCI individuals who cannot bear their body weight, would enhance the cardiorespiratory responses and muscle power production when compared to the normal ‘circular’ cycling pattern (4). This is due to the longer forward linear component of the motion, which allowed for effective, or should I say - efficient - quadriceps contractions. In normal cycling, the path is just too short for the muscle contractions to contribute. In short, the elliptical path provided greater dose-potency in the domain of FES-evoked cycling effectiveness.

Nevertheless, while all those factors would enhance the biomechanics and physiological responses of the SCI users, independently or in combination with each other, a crucial element that makes the system more ‘human’ is the feedback component. As in how our body works, our body always knows how much it has done, or the current state of itself in any domain of its working, in order to provide consequent signalling so that the final action is achieved or stability is maintained. The same principle is found in a common robotics or mechatronics system, where feedback is always present to provide optimal feedback control. In the case of FES, to date the most common mode of feedback reported is the electromyogram signal, or EMG, of the muscles (5). But you see, FES is electrical based, and so is EMG, and they are of the same muscle – they would ‘clash’ if simply used together concurrently. Of course, with proper signal processing these two signals can easily be split, and a lot of information can be extracted, especially muscle fatigue profile which is highly sought after to optimize performance.

Another way is to use power production indicator, simply the product of force production and speed, as the feedback parameter (6). In our developed FES ergometer the force and power are read from the end effector, which is through the foot pedals. This method provides a quantitative performance measure, and eliminates the need for extra wiring at the stimulated muscles – FES cables are messy enough for a fast, simple, day-to-day exercise activity. It also works on a primary domain other than electricity, thus careful signal processing and sensory attachment is less crucial. One possible drawback is the readings are at the end effector, and does not ‘look at’ or ‘reads’ the muscles directly, where the actual fatigue originates. One might think that to minimize fatigue, monitoring the power production might be too late or too far from the source of the problem and you cannot pinpoint which particular muscle requires attention most in terms of appropriate signal adjustment.

If there are other ways of directly monitoring the muscle contraction, without having the problems mentioned before, we would have an alternative feedback parameter to overcome or minimize fatigue optimally. When successful, the FES training device and the SCI user would be one complete system working in sync. The major problem of externally-stimulated muscle fatigue would be significantly delayed and the SCI person can gain hopefully maximum benefits of surface FES-evoked activity.

References


About the Author

Nur Azah Hamzaid obtained her PhD in Rehabilitation Engineering from the University of Sydney, Australia. She is currently a Senior Lecturer at the University of Malaya, Malaysia, with research activity in the field of biomechatronics. Her areas of interest include developing technical solutions for people with disabilities, such as functional electrical stimulation (FES) for people with spinal cord injury, smart prosthetic leg for lower limb amputees and smart toys for children with a disability. She works closely with spinal cord injured patients undergoing exercise rehabilitation using FES, and is actively developing and pursuing new FES technology for the benefits of the patients under the grant UM.C/625/1/HIR/ MOHE/ENG/39. She is also involved in Biomedical Engineering Prosthetics and Orthotics degree program development and coordination.
Stroke is one of the leading causes of long-term disability in developed countries, impacting not only stroke survivors, but also their family members, friends and caregivers. According to the National Stroke Association, some 40% of stroke survivors have moderate to severe impairments that require special care. Rehabilitation aims to promote maximum patient recovery, in order to enable the stroke survivor to attain highest possible levels of productivity and independence. The success of any stroke rehabilitation program depends on a number of factors, including the severity of damage to the brain, the patients’ motivation and willingness to do rehabilitative exercises, the skills of the physiotherapist and the period of time between stroke and commencement of the rehabilitation program. With latest technology advancements, the stroke rehabilitation scene is seeing another factor entering this mix – new therapeutic innovations, which help stroke patients recover in a more engaging and progressive manner.

Neuroplasticity and Stroke Recovery

However, before we look at some of these technology innovations, it makes better sense to understand the physiology of a stroke. A stroke happens when blood flow to the brain stops for a period of time, either due to a blockage of a blood vessel leading to the brain (known as ischemic stroke) or when the vessel becomes weak and bursts causing blood to leak into the brain (known as hemorrhagic stroke). The result of both types of stroke is that the brain cannot get blood and oxygen, causing some brain cells to die.

Although this damage to the brain is permanent, the brain has the capacity to change, re-organize and re-wire itself, in response to stimulation of learning and experience. This phenomenon is known as neuroplasticity, and replaces the previous belief that the brain is a static organ. This means that with the right stimulation, training and exercise, a stroke patient’s nervous system can generate new connections and pathways, leading to better recovery.
The brain is able to re-wire itself better when the following takes place:

1) **Intention-based therapy**: The neuroplasticity effect works best when the patient initiates the exercise and actively participates in the training session. This means that a physiotherapist cannot just move the patient's limbs through the required actions, but the patient must focus and take a driving role in the exercises. The more focus the patient has, the more rewiring occurs in the brain.

2) **Task-specific training**: This involves taking an activity that is done in everyday life, for example going out for a walk, and breaking it down into smaller more specific parts, for example, moving from sitting to standing, putting weight on the affected limb, or walking up a step. By focusing on specific and meaningful tasks, the patient's brain re-wires around the area of damage.

3) **High repetition exercises** – Practice makes perfect in the field of stroke rehabilitation. The repetition of an exercise reinforces and strengthens the brain's re-organization, until it becomes permanent, leading to better stroke recovery. This is because when muscles send signals to the brain again and again, they stimulate the brain to create new areas to receive and process these signals, which replace the areas damaged during the stroke. This is further reinforced when the patient continues to do the exercises at home on a frequent basis.

4) **Challenging exercises** – Typically intense therapies provide better rehabilitation. Challenging exercises builds strength, balance, flexibility and range of motion. However, while the training should not be too easy, it should not overwhelm the patient either.

Realizing the importance of these for areas to maximize neuroplasticity, physiotherapists usually develop a therapy program to combine them. So a therapy could involve intention-based, task-specific exercises that are repeated. In addition, as the patient shows progress, the intensity and duration increases, so that it gets more challenging.

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**New Technology Innovations**

As physiotherapists understand more about neuroplasticity, they are incorporating new advanced latest technologies to enhance stroke patients' treatment. One example is the Tibion Bionic Leg, the world’s first wearable robotic device that helps stroke patients to improve their gait and balance, strengthen stance and enhance active motor learning. The device, which is strapped to the patient's affected leg, consists of a pressure-sensing shoe insert, motors to provide leg support, an angle sensor in the knee and a computer for the therapist to program level of intensity and monitor patients' movements. When the patient applies weight, sensors in the device detect the force and motors support the leg by aiding the patient in ambulatory exercises. The Tibion Bionic Leg meets all four requirements for encouraging neuroplasticity. It is an intention-driven therapy, as the patient initiates the movement. The device supports task-specific exercises, such as sitting to standing movements, wall squats and climbing stairs. Patients are advised to participate in Tibion therapy twice a week for a minimum of six weeks, as well as to continue exercises at home, to ensure the repetitive reinforcement occurs. And as the patient's affected leg strength improves, the physiotherapist can reduce the level of assistance from the device. Another advantage of the Tibion Bionic Leg is that it is a portable wearing device. This is useful for in-patient cases, as the device can be brought to patient's bedside, and used to allow them to gain the first steps in regaining their mobility. This provides a psychological boost to the patient, helping to increase their motivational levels and confidence.

This motivational component of rehabilitation plays a key role in determining the success of a patient's mobility recovery. The ReJoyce Hand and Arm Rehabilitation System leverages upon this, through innovatively encouraging patients to do their rehabilitation exercises. The system includes a joystick-like Manipulandum, with features such as a gripper, peg, jar lid and door handle, together with a laptop to run
"...with the right stimulation, training and exercise, a stroke patient's nervous system can generate new connections and pathways, leading to better recovery." 

To motivate patients to use the Manipulandum in the right manner, the system runs games, which requires patients to carry out upper limb exercises. Games, such as target practice, driving simulations or pick-and-place, lead to different task-oriented exercises, which boost the patient's upper arm strength, flexibility, endurance and fine motor skills. As the patient progresses, the physiotherapist can adjust the games' difficulty levels to keep the games fun and challenging. This system can be delivered in clinic or as a home-based service, with the physiotherapist supervising the session via the internet. This makes it more convenient for the patient to exercise regularly, and the game element means that patients look forward to their therapy session.

The future of rehabilitation lies in how physiotherapists make use of their knowledge of neuroplasticity, as well as the readiness to incorporate new technologies, which will give stroke patients the best chance for recovery.

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Diana is the COO of Kinesis. She takes care of the running of the clinics in Singapore and overseas. Diana is also a physiotherapist by training and has many years of experience in the restructured hospitals before joining Kinesis. She specializes in incontinence treatment for women and believes that all women should be educated on incontinence treatment and prevention, and not suffer in silence. Diana also volunteers with museums as a guide on weekends and enjoys surfing the net for blogs on the latest food offerings and rushes to try them with her many "like-minded and like-passionate" friends.
An Impulse Radio Ultra Wideband System for Contactless Non-invasive Respiratory Monitoring

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Background

The use of ultra-wideband (UWB) technologies in medicine is an emerging research trend in recent years. Compared with X-ray imaging, UWB radar uses non-ionizing electromagnetic waves that are harmless to the human body. UWB signals offer high precision ranging on a sub-millimeter level, and are resistant to multi-path fading. This makes UWB a potentially cost-effective solution in medical diagnostics and monitoring applications like real-time localization and tracking.

After the US Federal Communication Commission (FCC) approved the limited use of UWB technology in 2002, UWB systems have drawn considerable attention for non-contact medical applications [1]. One important application is in sleep monitoring, where measuring the respiratory amplitude and breathing rate is crucial for sleep apnea diagnosis [2, 3]. Various UWB technologies have been studied, including frequency modulated UWB [4, 5], and impulse radio (IR) UWB [6-8].

In our recent research, we have used UWB to track the respiratory effort of human subjects in order to detect medical conditions like sleep apnea and other breathing disorders. Obstructive sleep apnea is the most common form of sleep breathing disorder, and occurs when there is partial or complete cessation of airflow due to upper airway obstruction, while ventilatory effort by the patient persists. Sleep apnea affects sleep duration and quality, leading to chronic partial sleep deprivation with consequent well-recognized impaired neuro-cognitive function and daytime performance, increased risk for metabolic and cardiovascular diseases (e.g. hypertension, coronary heart disease, life-threatening arrhythmias and stroke) and motor vehicular accidents [9-12], and a diminished quality of life. Large prospective cohort community-based studies have also added to the growing evidence that sleep apnea increases risk of death [13, 14].

In order to diagnose sleep apnea and other respiratory and sleep disorders, an overnight polysomnography (PSG) is performed in hospitals. Respiratory inductive plethysmography (RIP) is utilized for measuring the respiratory effort of the patient as shown in [15]. In RIP, elastic belts are worn around the chest or abdomen, and respiratory movements are measured by detecting the change in inductance of the belt due to the respiratory effort. This is an invasive technique for respiratory monitoring. Overtightening of the belts can

Figure 1: UWB respiration monitoring set-up.
impede the patient’s respiratory efforts, and shifting of body position during sleep often leads to loss of signals due to loosening of the belts. The belts also add to physical discomfort and may result in sleep disruption for the patient. The lack of adequate sleep time and loss of data signal may mean that the patient is required to repeat the PSG. Recently there have been new developments such as fabricating capacitive sensors in clothes, which can be worn by the patient in order to facilitate respiratory monitoring [16, 17]. However these methods may produce inaccurate results due to patient movements during sleep or other factors like ambient room conditions. Physical wear and tear of the capacitive sensors embedded in the fabric is also a challenge. Other methods involve the use of unobtrusive sensors and on-body wearable devices in order to measure the respiratory effort [18, 19].

A wireless, contactless and non-invasive respiratory monitoring system using IR UWB that can be used in PSG studies, home respiratory monitoring applications or other applications like physiotherapies has many advantages. The IR UWB signal has very large bandwidth, which facilitates high time resolution, and allows precise ranging estimation. Since human respiratory motion is on the order of millimeters, IR UWB is well suited for respiratory monitoring. In addition, the low power and non-ionizing properties of the IR UWB radar make it an ideal candidate for long time use. The use of IR UWB for estimating the breathing rate has been proposed by Lazaro et al. and Lai et al. [7, 8]. Their systems consist of two UWB antennas, one for transmission and the other for reception, and are pointed directly at the chest of the human subject. However, the performance of such systems is sensitive to the movement of the subject. Since one fixed antenna is used, if the human subject is not facing the antenna at a sufficiently small angle, the signal backscattering comes mostly from the side of the body instead of from the chest area, resulting in poor estimation accuracy.

Current Research on UWB Respiratory Monitoring

To solve the problem of the human subject not facing the UWB antenna at a sufficiently small angle, we propose a setup comprising of multiple UWB transceivers. Multiple transmit and receive antennas are placed at different locations to ensure that the backscattered signal can be detected by

![Figure 2: Estimated chest wall motion from our IR UWB system superimposed on the output from a RIP belt. Different colors for the IR UWB curve correspond to different state estimates for the subject facing direction $\rho(t)$.](image)
at least one receiver antenna no matter which direction the human subject faces. The system setup has been shown in Figure 1. One of the main challenges in such a setup is how to intelligently make use of measurements from all of the receiver antennas to estimate the respiratory motion. This process of "fusing" the information from multiple receiver antennas is done by a hidden Markov model (HMM) based method.

The HMM is a stochastic model in which the actual chest wall position of the subject is "hidden" from the system as the IR UWB system only indirectly measures the position by capturing the backscattered signal. By analyzing the backscattered signals from all antennas, we can not only estimate the chest movement, but also the direction that the human subject is facing. In addition, to help in automatic diagnosis of sleep disordered breathing, we have developed a method to segment the time series of chest wall motions into normal and abnormal breathing periods, based on their statistical characteristics.

We have verified the performance of our system and algorithms on 15 human volunteers. In our experiments, we compare the performance of our IR UWB system with the medical gold standard using RIP belts. It is found that on average, our estimation is over 81% correlated with the measurements of the RIP belt system. An example of the output from our algorithms is shown in Figure 2. The state $p(t)$ at time $t$ indicates the direction the subject is facing. In our experiments with two UWB transceivers, we discretize this direction into three possible states. In state $p(t) = 1$, the subject is facing antenna 1 directly, in state $p(t) = 2$, the subject is facing both antennas, and in the last state $p(t) = 3$, the subject is facing antenna 2 directly. The different colors in Figure 2 correspond to the different directions the subject is facing. It can be seen that our IR UWB system tracks the subject's wall motion and facing direction very closely.

**Conclusion**

UWB is a promising technology for use in medical monitoring and diagnostics. We have developed an IR UWB respiratory system that can track the chest wall motion of a human subject and her facing direction. This system improves on the current RIP belt method of measuring respiratory motion as it is contactless and non-invasive. The experimental results in this research have shown that the performance of our system is comparable to the performance of the RIP belt.

**References**


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Diagnosis of Alzheimer’s Disease Using Electric Signals of the Brain

A Grand Challenge

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I have recently been told that I am one of the millions of Americans who will be afflicted with Alzheimer’s Disease...” wrote the 40th president of the United States, Ronald Reagan, diagnosed with Alzheimer’s Disease (AD) at the age of 83. Presently, one American develops AD every 68 seconds, and by 2050 the rate is expected to increase to 33 seconds [1]. AD particularly affects the elderly population. In the United States, over 10% of people over age 65 and 50% of people over age 85 are affected by AD, and its prevalence is expected to triple within the next 50 years [2]. AD causes degeneration of the nervous system, leading to loss of memory, and reduced intellectual and social skills. No known cure exists for AD, however, progress is being made in drugs that slow its progression. As AD patients are elderly, their medical treatment is complex and costly compared to other diseases. Moreover, providing medical care for the AD patients is a difficult task where the caregivers undergo large physical and emotional stress.

In the preclinical stage of AD known as mild cognitive impairment (MCI) or predementia, the symptoms are not measurable enough, often ignored, and mistaken with the normal consequences of aging. Around 6% to 25% of the people affected with MCI progress to AD every year. The two first stages of AD, known as mild and moderate AD, are characterized by symptoms such as confusion, loss of language, and long-term memory loss. These cognitive deficits are so severe that it makes the patient withdraw from the social and family life, and become more dependent. In the final stage, known as severe AD, the personality deteriorates completely and the patients become entirely dependent on their caregivers. Once diagnosed positive, the average life expectancy of the patients is less than seven years. Between years 2000 to 2008, there was an increase in deaths due to AD by 66% [1].

Diagnosis of AD, particularly early diagnosis, is important for several reasons [3]. Most of the symptoms delaying medicines are effective when used in the early stage of the disease. Early diagnosis also allows effective treatment of psychiatric symptoms such as depression, which indirectly reduces the personal and societal costs of the disease. A positive early diagnosis gives the patients and their family the necessary time to understand the disease, to decide on the life and financial burdens of the disease, and to arrange for the future needs and care of the patients.

There is no specific test to diagnose AD directly; instead doctors often diagnose AD based on various tests to eliminate other possible causes [4]. These tests include simple physical and neurological examination, blood and spinal fluid tests, mental status tests, and neuropsychological tests. Increasingly, brain imaging techniques such as computerized tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET) are being explored for diagnosing AD. Apart from the mental and neuropsychological examinations, other examinations are either invasive or possess radiation dose (CT/PET), and/or are costly. There is a growing demand for AD diagnosis methods that are noninvasive, fast, inexpensive, and reliable. Electroencephalography has the potential to become such a diagnostic tool for AD.

We will now briefly elaborate on electroencephalography. The nerve cells, known as neurons, form the fundamental building blocks of the human brain, communicating among themselves (and other cells in the brain) by electrical and chemical signaling. The electrical signals among the neurons give rise to an electric field on the scalp, which can be measured noninvasively, and this recording is referred to as electroencephalogram (EEG). EEG is considered as “window of the mind,” as neurological diseases typically affect EEG in some specific ways. In recent years, many researchers have started investigating the potential use of EEG for diagnosing AD (see [3] for a review). EEG recording systems have become relatively inexpensive, compact, and mobile. Consequently, EEG can be recorded at the point of care (e.g., at home) at low cost, and hence EEG may potentially be used as a tool to screen a large population for the risk of AD. Though EEG signals often contain a wealth of information, the changes in EEG associated with AD are often not sensitive enough to show a clear differentiation, especially at early stages of AD. Significant research efforts are being made in improving the sensitivity of EEG in order to make it an effective tool for diagnosing AD.

According to the literature (see [3] for a review), AD perturbs EEG in three major ways. First, the EEG of AD patients becomes slower, in other words, more power in the EEG spectrum is concentrated at lower frequencies. Second, AD EEG contains fewer fluctuations, and hence it is considered less complex compared to healthy EEG. Third, EEG signals from different regions of the brain are less correlated in AD patients compared to healthy subjects. In the following, we briefly discuss those three characteristics of AD EEG.

Visual inspection of AD EEG shows an increase in diffuse slow activity compared to EEG of age-matched healthy subjects, which is confirmed by quantitative results from the computerized spectral analysis of EEG signals. Slowing in EEG, i.e., shift in spectral power towards low frequencies, is measured by calculating relative power in various EEG frequency bands. The frequency spectrum of EEG is often divided into non-overlapping frequency bands, such as 1–4Hz (delta), 4–8Hz (theta), 8–10Hz (alpha 1), 10–12Hz (alpha 2), 12–30Hz (beta), and 30–100Hz (gamma) [5]. A slight increase of power in delta and theta band has been observed in MCI EEG (see Fig. 1(a)), and this effect is more pronounced in the case of Mild AD (see Fig. 1(b)). In addition, there is typically reduced power at higher frequency bands (alpha and beta, 8–30Hz) in both MCI and Mild AD EEG. Interestingly, the strength of perturbations in the EEG spectrum has been shown to have an intricate relationship with the degree of progress of the disease [6].

EEG signals from healthy subjects are highly stochastic and fluctuate substantially, whereas AD EEG is often more regular and less complex. EEG complexity can be quantified in various ways [6]. Information theory [7, 8] provides a variety of complexity measures, including approximate entropy, sample entropy, Tsallis entropy and multiscale entropy. Entropy is a measure of the uncertainty associated with a random variable [7]. Some complexity measures have been developed in physics: fractal dimension, correlation dimension, and largest Lyapunov exponent. Fractal dimension is a statistical quantity that indicates how completely a
A fractal appears to fill space, as one zooms down to finer and finer scales. A fractal is generally a fragmented geometric shape that can be split into parts, each of which is (at least approximately) a reduced-size copy of the whole [9]. Natural objects that approximate fractals to a degree include clouds, mountain ranges, coastlines, and snowflakes. There are several definitions of fractal dimension; correlation dimension [10] is one of them. The Lyapunov exponent of a dynamical system is a quantity that characterizes the rate of separation of infinitesimally close trajectories [11,12]. The maximal Lyapunov exponent determines the predictability of a dynamical system. A positive maximal Lyapunov exponent usually indicates that the system is chaotic.

Many of the previously mentioned complexity measures, stemming from information theory or physics, have been applied to assess the complexity of EEG. Broadly speaking, complexity measures indicate the number of distinct patterns in the EEG signals. In earlier studies and our recent analysis [3,6], it has been observed that the complexity of MCI EEG is only slightly smaller than of healthy EEG. On the other hand, a significant loss in EEG complexity is noticed in the case of Mild AD patients, clearly indicating the progression of the disease. We conjecture that the loss of neurons and reduced anatomical and/or functional coupling among them makes the neural dynamics and hence observed EEG less complex.

An important effect of AD is the loss of interdependence among EEG signals recorded from different areas of the brain; this phenomenon may be due to the loss of coupling among the neurons. The synchrony between EEG signals can be measured in many different ways, ranging from linear (simple) measures to nonlinear (complex) measures [3,13,14]. Probably the most basic synchrony measure is the Pearson correlation coefficient; it quantifies linear correlations between pairs of signals. The (magnitude)
coherence function is an extension of the correlation coefficient from time-domain to frequency domain; it measures linear correlations in frequency domain [15]. Granger causality extends the correlation coefficient from pairs of signals to multiple signals [16]. It allows us to determine the causality of linear interactions. For instance, it is able to identify which EEG channels act as sources or as sinks. The approaches mentioned so far all focus on magnitude synchrony. Alternatively, one may investigate correlations between the phases of signals [17]. Indeed, the instantaneous phase of different signals may be strongly synchronized even if the amplitudes of those signals are statistically independent. An interesting alternative family of synchrony measures, referred to as state space based synchrony or generalized synchrony, stems from physics [18,19]. The signals at hand are assumed to be generated by some (unknown) deterministic, potentially high-dimensional, non-linear dynamical system. As a first step, one tries to reconstruct that system, by representing the signals in a state space: each signal is represented as a trajectory in that space. Signals are considered to be synchronous if their trajectories remain close to each other. A few years ago, we proposed an entirely different approach to quantify synchrony, referred to as stochastic event synchrony (SES) [20-23]; it characterizes the interaction between certain events in signals. In brain signals, those events can be spikes or transient oscillatory components.

The previously mentioned synchrony measures have been applied to AD EEG; we provide an overview in [3]. A large number of studies report a loss of EEG synchrony in MCI and AD patients. In most studies, a single synchrony measure is applied to a single EEG data set. Since almost every study considers a different measure and a different EEG data set, it is hard to compare existing studies and to verify whether results are consistent. To address this issue to some extent, we applied 35 synchrony measures to the EEG of MCI patients [14]. Most synchrony measures, especially Granger causality and SES, indicate a statistically significant loss of EEG synchrony in MCI patients compared to age-matched healthy control subjects. In another study [24], we repeated the analysis for EEG of Mild AD patients, and observed similar loss of synchrony in those patients. Those observations are in agreement with studies by other researchers.

In summary, EEG recordings may provide us valuable information for AD screening and diagnosis. Compared to other brain imaging modalities such as MRI and CT, which visualize the brain anatomy, EEG captures the fine-grain temporal variations of brain activity, and hence seems to contain signatures of abnormal brain dynamics of AD. Specifically, the effects of AD on EEG can mainly be divided into three phenomena: slowing, reduced complexity, and loss of synchrony.

In the following, we will briefly outline some of the challenges in using EEG as diagnostic tool for AD. As EEG signals are electrical potentials, they are affected by electronic interferences and contaminated by unwanted electrical potentials. For example, EEG recordings contain external interference from power lines, artifacts due to eye blinks, head movement, and muscle activity. Various signal processing techniques are being employed to selectively remove interferences and artifacts while preserving diagnostic features. However, identifying background noise from diagnostic information is subjective, and EEG experts do not always agree about EEG artifacts and their removal [3]. Instead of removing artifacts from EEG, it is often preferable to remove the portion of EEG with artifacts and use the rest of the EEG for analysis; however, this will lead to reduction in length of EEG and may reduce sample size significantly.

More problematically, the literature on EEG of AD patients is not always directly relevant for diagnostic purposes. As discussed so far, statistically significant perturbations in AD EEG have been observed in a plethora of studies. However, that does not immediately imply that EEG can serve as a diagnostic tool for AD. For that purpose, the EEG of individual AD patients should significantly differ from the EEG of healthy subjects and of other neurological patients. In most studies, however, effects across a population of AD patients are reported, and typically not on the level of individual patients. To address that issue, some researchers perform classification of AD and healthy EEG, where classification algorithms analyze a variety of EEG statistics, and decide in an automated fashion whether the EEG stems from an AD patient or a healthy person. As a rule of thumb, in order to be relevant for diagnosis, less than 20% of those decisions should be incorrect (classification error). It is crucial to determine reliable estimates of
the classification error. In many studies on classification of AD EEG, unreliable estimates of the classification error are reported, since the classifiers are trained and tested with the same data set. As a result, the classifiers may be over-fitted to the data at hand. Consequently, the reported classification results may not generalize to other data sets, and may be overoptimistic. To obtain more reliable classification results, one may for example apply cross-validation, as has indeed been done in a handful studies (e.g., [14, 25-31]). However, cross-validation only yields reliable classification rates if the data set is sufficiently large and the classifiers have a limited number of parameters.

To obtain more reliable classification results, one should ideally use three independent data sets [3]:

- The first data set is used to train various classifiers.
- The resulting classifiers are evaluated on the second data set; one retains the classifier with the best classification results on the second data set.
- The latter classifier is then evaluated on the third data set.

The classification results on the third data set are a reliable estimate of the actual classification performance, as long as the three data sets are sufficiently large and independent. At present, unfortunately, no databases of AD EEG are publicly available. Therefore, it remains hard to assess the potential of EEG for AD diagnosis. Progress in this area is hampered due to lack of access of large and independent databases of AD EEG. In contrast, such public databases are available for ECG [32], serving as a valuable test bed for ECG researchers worldwide.

In order to distinguish AD EEG from healthy EEG, it is recommended to analyze complementary EEG statistics. In other words, we advise to compute the correlation between various EEG statistics, and to select several uncorrelated EEG statistics for classification. As a consequence, the classifiers have access to complementary information to decide whether or not the EEG at hand stems from an AD patient. For instance, in a recent study [6], we discovered strong correlation between the phenomena of slowing and loss of complexity in AD EEG. We observed significant (anti-)correlations between relative power in various frequency bands and several complexity measures. As expected, combining relative power with complexity measures for classification of AD EEG vs. healthy EEG did not yield better results than classification based on relative power alone. On the other hand, several synchrony measures (phase synchrony, Granger causality, and stochastic event synchrony) did not seem to correlate with the relative power measures, and indeed helped to improve the classification results. Along the same lines, in our comparative study of synchrony measures [14], we observed that many synchrony measures are strongly correlated (either positively or negatively), as illustrated in Fig. 2. As a consequence, distinct families of synchrony measures may be identified. For example, from Fig. 2, it can be seen that SES is uncorrelated with all other synchrony measures, and hence it captures complementary information. This result suggests that it is not necessary to apply 35 or more synchrony measures for classification of AD vs. healthy EEG; it probably suffices to combine measures from each family.

It is also noteworthy that most of the studies on the diagnosis of AD using EEG are retrospective, i.e., they are based on the EEGs of already diagnosed subjects. So far, EEGs have not been used as a predictive tool, verified by the medical diagnosis to prove their effectiveness later. Moreover, most studies investigate how AD EEG differs from healthy EEG, whereas it also important to compare AD EEG with the EEG of other neurological patients. Another promising direction for future research is to leverage EEG with other brain imaging modalities and/or biochemical markers of AD. Although a few studies have explored such multimodal approaches, much research still needs to be done to gain further understanding in the neurophysiology of AD EEG, and its potential for AD diagnosis.

In conclusion, the EEG of AD patients has been investigated in a large spectrum of studies so far. Nevertheless, several critical bottlenecks and challenges need to be overcome before EEG can realize its potential as a noninvasive, fast, inexpensive, and reliable diagnostic tool for AD.

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VENTURE CHEMICAL LTD.
Finding the Right Partner
Transforming Pharmacovigilance Operations within Asia into Strategic Advantage

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For many Asian pharmaceutical companies, pharmacovigilance (PV) is a critical component of any drug development program. As product safety continues to receive a high level of emphasis for regulators, developers and the public alike, the need to effectively meet regulatory requirements, manage risk and process safety reports remains a key foundation of pharmaceutical development in Asia.

However, a number of conflicting trends have emerged regarding PV strategy and operations for Asian firms in recent years. Regulatory bodies across the region are intensifying safety regulations even as they work to reduce approval times and accommodate to the explosion of activities in the region. As a result, companies are receiving growing numbers of safety reports despite a trend towards reducing staff in their PV operations. At the same time, many companies opt to retain in-house PV staff while a wide range of other pharmaceutical operations increasingly become candidates for outsourcing and offshoring. Together, these and other trends result in increased costs and slower processing times for PV operations.

Much like their counterparts elsewhere in the world, many Asian pharmaceutical executives view PV primarily through the lens of cost, even as they recognize the value of carefully managing a product’s safety profile. This perspective leaves companies struggling to achieve a balance between high productivity, short cycle-times and high quality. For other components of the development process, the solution may well be found in outsourcing. Yet, due to the critical nature of analyzing and processing safety data, many companies are reluctant to turn to outsourcing as a solution.

The Need for Balance

To meet the requirements of a demanding and changing regulatory and development landscape, Asian pharmaceutical firms must view PV operations as more of a strategic opportunity and less a mandated cost center. To accomplish this transition and effectively position themselves for the future, developers must identify a pathway that addresses both quality and productivity while also minimizing risk, adapting to fluctuations in demand and creating strategic value from carefully managing the safety profile of a product.

Of course, the challenges inherent in strategically positioning PV to create value are many. For one, language barriers and complex regulatory environments make Asia one of the most challenging markets for developers to achieve regulatory compliance.
Within such a complex environment, managing data collection processes involving multiple non-clinical sites with non-physician medical reviewers can prove to be a significant logistical and data collection challenge. Further, lesser rates of electronic data capture and computer-based analysis than elsewhere around the globe force many companies to choose between devoting scarce resources away from strategic interactions with health authorities and developing innovative treatments and more towards day-to-day document and data management.

Perhaps most importantly, however, stands the need for Asian developers to ensure the highest levels of quality around drug safety reporting and risk management, to both meet regulatory guidelines and to effectively shepherd drug development and commercialization. For example, many companies struggle with the ongoing potential for high levels of non-compliance risk from increasing numbers of case reports and changes in regulatory requirements. Developing timely and effective medical assessments, signal detection, medical review, case monitoring and other vital processes and analyses are critical components of successful PV. As firms face the danger of non-compliance which can even place the status of their development and commercialization efforts in jeopardy due to late or incorrect regulatory filings, many developers choose to place strict controls on all PV operations and mandate in-house capabilities whenever possible.

A Mandate for Quality

Yet, within the overall landscape of regulatory changes, clinical trial management and technology solutions, opportunities to develop more strategic PV processes exist. Today, many multinational pharma companies have developed partnerships with clinical research organizations (CROs) within Asia to help develop and manage PV operations and strategies. Further, the use of both outsourcing and offshoring across a wide range of clinical trial activities beyond PV has grown considerably in recent years for both domestic and global developers alike. More promisingly, hurdles to processing documents and data across language barriers are falling, as an increasingly talented workforce and advanced expertise are being developed at a rapid pace across Asia.

For firms that place a premium on both quality and productivity, finding a CRO to serve as a strategic partner can be difficult. For many developers, the bulk of work currently being outsourced to outside providers is centered primarily or exclusively around lower-level data entry and site management tasks. For maximum success, however, a PV services provider must be able to successfully manage complex data collection processes inherent in large studies involving multiple non-clinical sites, possess a deep understanding of regional regulatory requirements and offer the highest possible
"...a PV services provider must be able to successfully manage complex data collection processes inherent in large studies involving multiple non-clinical sites, possess a deep understanding of regional regulatory requirements and offer the highest possible levels of data management quality and language capabilities."

levels of data management quality and language capabilities. Further, service providers must be able to ramp-up resources quickly to accommodate a developer’s workflow needs, be able to demonstrate productivity and efficiency gains on a year-over-year basis and provide a transparent platform that allows a developer insight and control as needed to all phases of PV operations.

The Opportunity for Strategic Value

In order to truly become a strategic partner with pharmaceutical developers in turning PV operations and processes from a cost center to a strategic advantage, a CRO provider must first and foremost be able to ensure that quality and compliance will not suffer as a result of transferring PV work away from a developer’s in-house staff.

Recently, Quintiles launched a Center of Excellence (CoE) in Dalian, China, to further the drive for increased productivity, lower costs for PV and back office support for pharmaceutical firms in Asian geographies. With a highly trained staff and a wide range of expertise in case processing and handling, the Dalian location can lower PV costs by as much as half over accomplishing the same tasks in-house.

Quintiles stands uniquely qualified to provide Asian firms the support and cost savings they need to move PV processes from regulatory mandate to strategic advantage. Designed to work directly to the highest quality standards, the Dalian CoE builds on Quintiles’ years of project management, quality assurance and clinical trial experience, along with a management and technical staff who have built credibility with investigators and regulatory authorities across the region.

For firms able to identify the right partnership, the opportunity exists to help differentiate their products from the competition by increasing its value through lower costs and streamlined development processes. In fully capturing a product’s safety profile without committing a wealth of resources or diverting focus from other critical processes, pharmaceutical firms across Asia can transform their PV efforts from a costly, mandated process to a strategic asset that creates value and helps deliver innovative products to patients with fewer hurdles, higher quality and increased safety.

About the Author

Siew-Ping is Senior Regional Director and Site Head of Lifecycle Safety for Quintiles in Asia Pacific. She is based in Quintiles’ regional headquarters in Singapore and leads a team of more than 120 dedicated safety specialists based in Singapore, Japan, India and China. Her team in Asia-Pacific specializes in integrated safety services across entire drug lifecycle from Phase 1 to 4 clinical trial safety, to post-marketing safety, risk management and safety insights. As a core member of the Quintiles global executive safety team, Siew-Ping is responsible for developing and implementing Quintiles’ integrated drug safety and risk-management strategies in Asia-Pacific markets.

Siew-Ping graduated from the School of Pharmacy in National University of Singapore. She has worked as a hospital pharmacist before joining Quintiles Drug Safety in 1998. With more than 14 years of experience in the drug safety industry, Siew-Ping has an in-depth knowledge of pharmacovigilance practices both globally and in the Asia-Pacific region. She is also well-versed in safety reporting requirements of the regulatory agencies in the Asia-Pacific region.
I n the US and European economies, the past four years have been testing for many biotech companies and the future remains uncertain. In addition to a tougher operating environment, companies have to cope with the difficulty of raising funds and signing deals with larger, better-resourced, global firms. Despite all the challenges, some biotech companies have managed to adapt to the situation and navigate around various obstacles to achieve their goals through ‘outsourcing’ strategies.

The German biotech company, BioCrea, discovers and develops novel drugs for the treatment of debilitating central nervous system diseases such as Schizophrenia and Huntington’s disease. Its discovery efforts are focused on the recent finding that brain phosphodiesterases (PDEs) are key regulators of response and plasticity of the brain. Processes like memory and learning are associated with PDE function, as are dopamine- and glutamate-related signals, which are altered in diseases like Schizophrenia. The company was set up in 2010, comprising a team with a strong track record in science, business development and commercialization. Despite these advantages, BioCrea, like their counterparts in Europe and elsewhere, had to cope with a difficult fund-raising and deal-making climate. Still, the company was able to successfully conclude an asset purchase and licensing deal with a global partner for its unique PDE platform in the first quarter of 2012.
Dr Thomas Kronbach, CEO of BioCrea, credits the firm’s recent success on the management team and support from external scientific and business development experts, which were brought in as consultants, to further strengthen the company’s reach and capabilities. He explains, “Our consultants have extensive experience and deep knowledge of the industry. Furthermore, they have access to a wide network of contacts in the pharmaceutical and biotech sectors.” According to Dr Kronbach, BioCrea’s consultants have allowed the company to operate very efficiently in reaching potential partners. He added, “As we are a small biotech company, we have limited resources that we have to utilize carefully. Working with consultants has allowed us to reach targets through their networks, giving us the opportunity to link up with potential partners. The consultants not only make the initial introductions but also ensure that the interactions between BioCrea and its partners proceed smoothly. They are there with us when we present our technologies and support us in drafting the contracts and closing the deal. If we had to do this alone, it would have taken longer and probably would have involved employing more senior managers in the long term. With that perspective in mind, the perception that consultants are “expensive” turns into “good value for money” because the assignment is tailored to the needs, resources and timelines of the company.”

BioCrea’s business development consultant is Dr Juergen Parrisius who has been an independent consultant since 2003. Prior to that, he has over 20 years’ experience in international marketing and business development at companies such as Pfizer, Roche and Cardion. His role at BioCrea was to plan and initiate the partnering process and to run the process smoothly with frequent reporting to the BioCrea management team.

According to Dr Parrisius, the practice of using consultants in Europe and US is quite common as it allows companies to quickly tap into additional resources and expertise without incurring long-term overheads. However, Dr Parrisius cautions that using consultants is still only part of the answer. He explains “good business development and good technology have to go hand-in-hand, and I have been able to help BioCrea because it has fundamentally outstanding technologies and a strong team that allows me to present the company in the right way, to the right people, at the right time. All the pieces have to come together.”

Similarly, one company in Asia that has reaped the benefits of using external consultants is Cerca Insights, a Contract Research Organisation (CRO) based in Penang, Malaysia, which specializes in behavioural pharmacology. The company was set up in 2008 with the core focus of helping its clients to improve their drug discovery productivity. Cerca Insights now conducts a wide range of paradigms that can assess neurological and cognitive functions along with behavioural toxicity, and it has successfully leveraged the economics of Malaysia to deliver value to its international clientele.

CEO of Cerca Insights, Mr Anthony Bishop explained, “We are a Malaysia-based company that serves the global market. In our business, building relationships with clients and potential clients is very important. For a start-up company, there is never enough time for that when we are not geographically close to the markets that we serve. Fortunately, we are able to work with experienced consultants who are able to guide us and connect us to our markets. Working with them also allows us to cut short the time needed to establish a good working relationship with potential clients.” The company’s consultants were former senior executives of global pharmaceutical companies and were able to augment Mr Bishop and his team with the capabilities to rapidly grow the business.

Like external consultants, interim managers are usually senior personnel who have a successful track record in a particular area. Interim managers work through interim management companies that provide them with specific assignments at an organization for a particular project for a specific length of time. Ms Susan Macdonald is the Managing Director of RSA Singapore, a global life sciences executive search and interim management firm. She noted that “Currently, the practice of using interim managers and external consultants is still less common in Asian based companies compared to the US or Europe. For example, SMEs in the region tend to want to use their own internal resources as there is a perception that external interim managers are an expensive solution.” Ms Macdonald added “However, the industry in Asia is maturing and more companies in fast emerging life sciences markets like China are recognizing the benefits of using interim managers as they become more familiar with the practice and the cost-benefit balance that these experts bring to the table.”

As life sciences companies in Asia mature, they will inevitably pick up industry best-practices from companies elsewhere as well as develop new strategies to adapt to the highly competitive global market. Tapping on external expertise will become an integral part of their business practices.

**About the Author**

Marvin Ng is the Managing Director of DN Venture Partners LLP, a life sciences business development consulting firm which he set up in 2001 to help companies to expand their business, manufacturing and research activities in Asia. Marvin is a microbiologist by training but has experience in various fields including international marketing, business development, fund raising, and investment/trade promotion. For more information, please visit www.dn-venture.com.
Agilent Technologies licenses SureFISH to BioDiscovery

Agilent Technologies Inc. announced that it has entered into a licensing agreement with BioDiscovery, Inc., enabling BioDiscovery customers to access Agilent SureFISH probes directly from BioDiscovery’s Nexus software. Researchers using a variety of cytogenetic microarray platforms can now quickly identify aberrations via Nexus to immediately identify and link to available oligonucleotide-based fluorescent in situ hybridization (FISH) probes for follow-up studies.

“We are pleased to provide this comprehensive real-time solution to cytogenetic researchers,” said Kathleen Shelton, Agilent’s director of marketing for genomics. “This cooperative agreement demonstrates yet another way in which researchers can leverage our comprehensive, user-friendly SureFISH platform, allowing them to complete their studies more efficiently and effectively than before.”

Agilent’s SureFISH probes are designed for specific, nonrepetitive regions of the genome, enabling users to detect repetitive or aberrant regions as small as 50 kb. This design also reduces the hybridization time to as little as four hours. With a continuously growing menu of SureFISH translocation probes, all centromere probes, 35 telomere probes, and more than 400 general-purpose probes, BioDiscovery customers will be able to efficiently identify probes of interest without having to search external websites and catalogs.

“BioDiscovery Nexus users deal with the full spectrum of cytogenetic platforms,” said BioDiscovery vice president for business development Louis Culot. “We are excited to be able to connect SureFISH seamlessly with Nexus, directing users to probes of interest while they conduct their sample analyses.”
Bionomics acquires US-based cancer stem cell company Eclipse Therapeutics

Bionomics Limited announced its acquisition of San Diego-based private biotechnology company Eclipse Therapeutics Inc (Eclipse) in a scrip-based US$10 million deal. With consideration of approximately 23.9 million shares at 41.76 cents per share, Eclipse shareholders, that include NASDAQ-listed Biogen Idec, will own approximately 6.5% of Bionomics’ issued capital.

A spin-off of the Biogen Idec Inc oncology franchise, Eclipse is developing drug candidates that target cancer stem cells (CSCs). CSCs are the seeds at the root of the cancer, and CSC technology is thus viewed by many oncologists and pharmaceutical companies as a high priority, new oncology drug frontier.

Eclipse’s lead compound ET101 is aimed at an undisclosed CSC target which is over-expressed on most solid tumors. ET101 is expected to move into human trials in 2014. In March 2012 Eclipse reached a development and manufacturing agreement for production of the ET101 antibody with Swiss life science leader Lonza Group Limited.

“This acquisition elevates and expands Bionomics’ oncology pipeline beyond BNC105, our primary cancer drug candidate which is now at advanced clinical stages. It also establishes Bionomics as a global leader at the forefront of cancer stem cell therapeutics,” said Dr Deborah Rathjen, CEO and Managing Director of Bionomics.

“CSC companies in the US have not only attracted the interest of public biotech investors (evidenced by Verastem’s NASDAQ listing at a market capitalization exceeding US$200 million) but also interest from large pharmaceutical companies (evidenced by the significant partnering deals done by OncoMed with GSK and Bayer combined value of approximately US$3.4 billion).

“The Eclipse acquisition will provide Bionomics with an important strategic base in the US, the world’s largest pharmaceutical market.”

Since 2004, significant resources have been invested in Eclipse’s CSC drug program. Eclipse’s CSC Rx Discovery™ platform has been used to identify antibody therapeutics that inhibit the growth of CSCs.

Scientific and clinical research supports the concept that CSCs are responsible for tumor initiation and recurrence. Cancer stem cells tend to be resistant to chemotherapy and other conventional forms of cancer treatment.

Eclipse was founded by former Biogen Idec employees Dr Peter Chu and Dr Christopher Reyes along with Dr Jonathan Lim, managing partner of City Hill Ventures and includes a world class team of scientists.

Dr Lim has been appointed a Non-executive Director of Bionomics.

“Eclipse shares Bionomic’s vision of building a world-class oncology franchise, and integrating our oncology assets with Bionomics strengthens our prospects for success based on their existing depth of oncology expertise and ability to be part of a larger and highly motivated team”, said Dr Lim.

Dr Peter Chu and Dr Chris Reyes have taken up the positions of Vice President US Operations and Cancer Biology and Vice President R&D Biologics respectively for Bionomics.

In addition to acquiring Eclipse’s world class assets, Bionomics’ expansion into the US will enable it to benefit from a number of synergies as well as bring greater profile to its business development activities and accelerate its small molecule and antibody programs.

Eclipse shareholders may qualify for cash earn-outs based on achieving late stage development success or partnering outcomes based on Eclipse assets. Eclipse has a strong intellectual property position in CSCs. It acquired Biogen Idec’s patent applications covering the isolation of CSCs for drug discovery and has continued to expand its portfolio of product-related patent applications.

Bionomics’ Chairman Mr. Chris Fullerton said, “Bionomics is a company that continues to marry a high value drug development pipeline with strong commercial partners and pathways. Despite difficult financial markets our company signed the ground-breaking US$345 million Ironwood anxiety therapy deal, expanded and accelerated our Kv1.3 program with new targets, initiated a BNC105 ovarian cancer clinical trial and has now grabbed a foothold in a highly promising cancer stem cell technology.”

“With the acquisition of Eclipse, Bionomics also achieves a key corporate goal of establishing a meaningful and prospective presence in the US”.

For the purposes of ASX Listing Rule 3.10.3, Bionomics’ advises that it proposes to issue a maximum of 23,890,718 fully paid ordinary shares (ranking equally with ordinary shares on issue) at a price of 41.76 cents per share to Eclipse shareholders in connection with the transaction described above (no shareholder approval will be sought in relation to this proposed issue). Recipients of the shares are bound by escrow arrangements which extend from 6 to 12 months.
AB SCIEX announces Biologics Initiative

AB SCIEX announced on a global initiative focused on biologics. This new initiative is in response to the fundamental shift of the pharmaceutical industry into biopharmaceutical development. AB SCIEX’s BiologicsFocus Initiative consists of four components: new product development; beta software evaluation program; one-on-one connections program; and forums for sharing the latest advancements in biologics across the scientific community. The company revealed this initiative at the International Mass Spectrometry Conference (IMSC) in Japan.

The BiologicsFocus Initiative represents AB SCIEX’s open approach to producing comprehensive biologics solutions by involving scientists in industry and academia in the development of new tools. AB SCIEX already has a proven track record with its TripleTOF technology for bio-therapeutics characterization. The company is now taking the next important step to address an industry-wide need – the development of data analysis solutions to simplify and accelerate biologics development.

42% of new drugs in drug development pipelines of pharmaceutical companies are based on biologics, according to survey results published earlier this year by EvaluatePharma, a market research firm. Moreover, the development of biosimilars, or “generic” biologic drugs, is dramatically increasing globally in response to legislation enabling their licensure in the United States.

The trend is to transition away from the traditional model of drug development, which is based on small molecule analysis. The promise of biopharmaceuticals is that pharmaceutical companies will be able to more rapidly develop more effective drugs with fewer side effects. Recent advancements in technologies for large molecule analysis, such as protein characterization, have sped up the shift to bio-therapeutics.

AB SCIEX’s biologics Initiative includes the following programs:

• **BiologicsFocus Innovation** – AB SCIEX is developing a suite of new products specifically for biologics. Because data analysis is considered to be a bottleneck for this type of analysis today, the company is focusing on software development in the first phase of this initiative to eliminate this bottleneck.

• **BiologicsFocus Eval** – AB SCIEX is actively developing new biologics characterization software.

• **BiologicsFocus Summits** – AB SCIEX will host information-sharing forums or "summits" as special events that will bring together opinion leaders who are driving the evolution of biopharmaceuticals. This will also include an advisory network of scientists to provide input and feedback for ongoing product development.

• **BiologicsFocus Connections** – AB SCIEX will connect biologics researchers one-on-one with each other to cultivate new collaborations and advance this field of pharmaceutical science.

“We recognize biologics for its strategic importance to the pharmaceutical industry,” said Rainer Blair, President of AB SCIEX. “AB SCIEX is well-positioned with our industry-leading hardware platforms and our unique combination of strengths in both large molecule characterization and pharmaceutical analysis. We are working closely with pharmaceutical scientists to develop and shape new software solutions that directly address the needs and requirements for the new frontier of drug discovery and development. We continue to be a trusted partner with pharmaceutical companies and academics worldwide.”
Phylogica licences skin-repair peptide to Le Métier De Beauté for cosmetic market

Phylogica Ltd announced on that it has licensed its skin-repair Phylomer® peptide PYC35 to Le Métier de Beauté for use in cosmetic products in the US, UK and Hong Kong markets.

Le Métier will use PYC35 in its premium range of Peau Vierge anti-aging creams that will be commercialized initially across the US through department stores such as Neiman Marcus, Bergdorf Goodman and Nordstrom. Le Métier is responsible for all future costs including formulation, manufacturing and marketing.

Under the terms of the agreement Phylogica will receive a significant royalty on all sales of Le Métier’s cosmetic products that contain PYC35. Phylogica retains all pharmaceutical rights to PYC35.

The Phylomer peptide PYC35 derived from the genome of a microorganism known as Pyrococcus horikoshii, which belongs to an ancient kingdom of life that evolved billions of years ago. This thermophilic species dwells in undersea volcanic vents and can endure extreme environmental conditions such as high pressure and high temperature. In these environments the pressure is about 200 atmospheres with temperatures of nearly 100°C.

The properties of the PYC35 peptide reflect some of the unique characteristics of its host species. In preclinical models of dermal wounds, UV radiation damage and severe skin burns; PYC35 showed potent skin-repair activity. For example PYC35 significantly improved the process of wound healing in a well-validated model of severe skin burns. The potential cosmetic applications of PYC35 include use in treatments to repair skin following sun or thermal damage and in a rejuvenating serum to reduce skin damage from long-term environmental exposure to UV.

Le Métier’s Chief Executive Officer Richard Blanch commented on the news: “Le Métier de Beauté is very excited to license PYC35 from Phylogica. There is genuine demand from our client base and retail partners for products that can prevent scars and repair skin from the sources of damage such as UV exposure. Le Métier plans to use PYC35 within its Peau Vierge product range to develop groundbreaking new cosmetic and skincare products for the luxury beauty marketplace.”

Phylogica’s Chief Executive Officer Dr Paul Watt added: “We are delighted to have licensed our PYC35 peptide to Le Métier de Beauté as an active ingredient in its high-end range of cosmetics. Given the exotic habitat of Pyrococcus which dwells in the harsh environment of undersea vents, it is intriguing that a peptide derived from that organism’s genome has potential in repairing burn injuries and preventing long-term skin damage such as scars.”

“While we expect to announce new alliances in the coming months relating to our core drug discovery, this cosmetics deal opens up a new market opportunity and could generate meaningful near-term revenue for Phylogica. This deal with Le Métier is non-exclusive and we are evaluating other opportunities to maximise the market opportunity for this peptide.”
Brooks' Single-use REMP tubes support optimization of automated serum and plasma storage

Brooks Life Science Systems, a division of Brooks Automation Inc., announced that Karolinska Institute Biobank (KI Biobank) is successfully using Brooks’ REMP single-use heat sealed sample tubes to secure the long-term storage of plasma, serum, and urine samples in its automated biorepositories.

Brooks has worked with the biobanking experts at KI Biobank to support the development of a best practice workflow which minimizes freeze-thaw cycles and sample contamination. Brooks’ REMP single-use tubes were successfully integrated into a novel robot-driven automated workflow that offers maximum sample security within a temperature controlled environment to ensure the long-term availability of high quality biological samples to support biomedical research.

With hospitals and research institutes around the world building collections of biological samples as a resource for biomedical research, these biorepositories must be able to guarantee the long term, secure storage of vast sample sets. A number of studies (1, 2) have demonstrated the importance of minimizing freeze-thaw cycles and the negative effects of repeated sample exposure to the quality of blood serum and plasma samples.

Clint Haris, Vice President, General Manager, Brooks Life Science Systems added: “The adoption of single-use tubes by such a prestigious organization is validation of Brooks’ technology and we are very proud to be part of this collaboration. The development carried out by the team at the KI Biobank will help ensure a focus on sample integrity and set the standard for secure biological sample processing.”

Brooks’ REMP tubes address the key issues faced in biorepository sample management by providing a format that enables tubes to be picked and thawed once, avoiding repeated freezing and thawing and potential for contamination. In addition, the use of heat sealed tubes can save space and offer higher sample integrity at low temperatures versus alternative solutions.

Genetic Technologies announces key managerial appointment
Mark Ostrowski to head-up US sales for BREVAGen™

Genetic Technologies Limited announced on the appointment of Mr. Mark Ostrowski as Senior Vice President Sales & Marketing Molecular Diagnostics. In this role, Mr. Ostrowski will be responsible for managing the US sales effort for BREVAGen™, the company’s cornerstone commercial product.

Prior to joining Genetic Technologies, Mr. Ostrowski’s career spanned both early stage and established biomedical companies. During his tenure at Myriad, he had comprehensive exposure to all aspects of sales and marketing, managing a sales force of over 200 representatives, demonstrating average annual revenue growth of over 50%, and generating new strategic divisions and best practice policies.

“I’m excited by the opportunity to join Genetic Technologies and to spearhead BREVAGen’s™ commercialization efforts. I am looking forward to applying my experience in oncology and women’s health diagnostics to BREVAGen™, which I feel has the potential to be a keystone product in the evolution of breast health,” said Mr. Ostrowski. “The recent approval to sell BREVAGen™ within the state of California has provided access to a material segment of the US market. With New York and Florida approvals on the horizon, I see a tremendous opportunity to leverage these significant milestones into increased national adoption for this important test.”

With the successful establishment of the Company’s US infrastructure over the past two and a half years, culminating in the launch of BREVAGen™, the Company is now sharpening the focus of the US organization around sales and centralizing support activities in Australia. As a result, the leadership of the US sales and marketing group will be transitioning to Mr. Ostrowski. Mr. Lewis Stuart will be assisting the company in a strategic advisory capacity during this process.
### NOVEMBER 2012

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<td>International Conference on Speech, Image, Biomedical &amp; Information Processing (SIBIP 2012)</td>
<td>Punjab, India</td>
<td>Shivani Malhotra</td>
<td>+91 98884 92132</td>
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<td>7 – 8 Nov.</td>
<td>4th International Conference on Science &amp; Technology (ICSTIE)</td>
<td>Penang, Malaysia</td>
<td>Azlina Mohd Mydin</td>
<td>+604 3823373</td>
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<td>26 – 27 Nov</td>
<td>BioPharma India Convention 2012</td>
<td>Punjab, India</td>
<td></td>
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### DECEMBER 2012

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<td>Dr. Dilbag Singh</td>
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<td>14 – 16 Dec</td>
<td>International Medical Congress</td>
<td>Phnom Penh, Cambodia</td>
<td>Dr Anbin Ezhilan</td>
<td>+855 092-526647</td>
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<td>22 – 23 Dec</td>
<td>2012 4th Journal Conference on Bioscience, Biochemistry and Bioinformatics (JCBBB 2012 4th)</td>
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<td>27 – 30 Nov</td>
<td>Pharma Anti-Counterfeiting &amp; Brand Protection Asia 2012</td>
<td>Singapore</td>
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<td>+65 6508 2401</td>
<td>+65 6508 2407</td>
<td><a href="mailto:register@ibcasia.com.sg">register@ibcasia.com.sg</a></td>
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**JANUARY 2012**

3 – 5 January  
Good Clinical Laboratory Practices (GCLP), 2013  
Chennai, India  
Contact Person: Mr. J. Mohanakrishnan, M.Sc; Mr. P. Nandagopalan, M.Sc  
Tel: 39106800 / 39106803  
Email: GCLP@yrgcare.org  
URL: http://www.yrgcare.org/gclp/index.php

8 – 10 January  
2013 International Congress on Chemical, Biological and Environmental Sciences  
Taipei, Taiwan  
Contact Person: Chandra Nale  
Email: iccbs@iccbes.org  
URL: http://www.iccbs.org

11 – 12 January  
European Society of Endocrinology (ESE) Clinical Update 2013  
Abu Dhabi, United Arab Emirates  
Contact Person: Kate Sargent  
Tel: +44 01454 642240  
Fax: +44 01454 642222  
Email: conferences@bioscientifica.com  
URL: http://www.e-se-hormones.org/meetings/2013/esecu2013/

19 – 20 January  
3rd International Conference on Life Science and Technology (ICLST 2013)  
Dubai, United Arab Emirates  
Contact Person: Ms. Yang  
Email: iclst@iccbes.org  
URL: http://www.iclst.org/

19 – 20 January  
2013 International Conference on Scientific Research and Studies (ICRS 2013)  
Dubai, United Arab Emirates  
Contact Person: Jason Wu  
Tel: +61 820 7777775 (China)  
Email: icrs@sci.org  
URL: http://www.icrs.org/

**FEBRUARY 2012**

4 – 6 February  
Bangalore India Bio  
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