BIOTECHNOLOGY IN Thailand

Take a closer look at Thailand...
the land for bio-investment

Contents

Articles and information in this publication were contributed by:

National Science and Technology Development Agency (NSTDA)

Board of Investment (BOI)

Market for Alternative Investment (mai)

Technology Management Center (TMC)

Mahidol University

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DOING BIO-BUSINESS IN THAILAND

WHY THAILAND?

Market Access

The combination of Thailand's abundant natural resources and skilled workforce provides investors with the critical inputs for successful ventures, which are enhanced by additional support from the Thai government in key sectors. These prioritized sectors include automotives, ICT/ electronics, agriculture, fashion, alternative energy, biotechnology and high value-added services. The country also fares well when specific manufactured products are examined. For example, Thailand is the world's prime producer of natural rubber as well as a top exporter of rice, shrimp, canned and frozen seafood and canned tuna, along with canned pineapples and cassava. The country is also the second major exporter of sugar. Thailand leads the world in manufacturing hard disk drives, with over one third of the world market, and is also well on the way to being among the top-ten auto manufacturing countries.

Thailand is strategically located in the heart of Asia, with easy access to some of the world's most dynamic markets as well as a domestic market of 65 million people. Its attractiveness as a production base for leading international companies is further enhanced by the host of Free Trade Agreements (FTA) or Early Harvest Schemes signed by Thailand that provide such advantages as duty-free imports of raw materials and components, as well as duty free access to markets around the world. Thailand has already signed agreements with countries such as China, India, AFTA, Japan, New Zealand and Australia.

Thailand's Board of Investment

The BOI under the Ministry of Industry is the principal government agency for encouraging investment. If you wish to set up an operation in Thailand, the BOI is available to assist you in enhancing your competitiveness and facilitating your investment by:

- Offering an attractive and competitive package of tax and non tax incentives.
- Imposing no foreign equity restrictions on manufacturing activities or on some activities.
- Providing assistance in the provision of visa and work permits to facilitate entry and subsequence operation for a foreign-owned business.
- Waiving restrictions on land ownership by foreign entities.

In addition, the BOI provides business support services such as comprehensive information and advice on establishing operations in Thailand, arranging site visits, identifying potential suppliers, subcontractors, joint-venture partners, providing useful contacts with key public and private organizations and coordination between the foreign business community and other public agencies.

Biotech activities that are granted special tax investment incentives by the Board of Investment should involve research and development and production requiring a high level of biotechnology within the following four areas:

- Seed production or plant and animal improvement.
- Medical supplies such as vaccines.
- Testing kits for medical, agricultural, food and environmental use.
- Microbe, plant cell and animal cell use to produce biomolecules and biologically active compounds.

On April 9 2007, the biotechnology sector was granted the highest promotion privileges by the BOI. These privileges include import tax exemption for machinery/ equipment and a personal income tax exemption for 8 years without limit for every zone. Corporate income tax for net profits will be reduced by 50% for an additional 5 years if the bio-business is located in the Thailand Science Park.

For more information, please visit http://www.boi.go.th.

Ease of Living

Looking beyond the country's industrial attractiveness, when it comes to lifestyle there are few countries who can combine the above environment with a low cost attractive lifestyle. The Mercer Human Resource Consulting Cost of Living Survey (worldwide ranking 2008), places Thailand far down the list at no. 95. Thus, not only can individual business excel in Thailand's business environment, but family members too will benefit and prosper from the experience. Thailand offers the expatriate community among the best international schools in Asia.

In addition to a commitment to excellence in education, Thailand prides itself on an excellent national cuisine that is enjoyed the world over. There is also a wide selection of restaurants offering an international menu with everything from European to Chinese cuisine to choose from. So no matter what the palate, eating and enjoying a meal in Thailand is not another chore, but a way of life and a good way to do business. And for those just looking for leisure can expect world class shopping complexes, beach and mountain resorts, hotels and golf courses.

Modern Infrastructure

For over two decades, successive Thai governments have understood the importance of infrastructure in creating attractive investment conditions. Industrial estates and parks in all major regions are linked by road, rail and air. The system includes seven international airports, a rail system linking neighboring countries such as Malaysia and Singapore, river transport linking with Laos, Myanmar and Southern China and a series of eight large container ports linking with the rest of the world.

STANG HOLDING
Mahidol University Group

Mahidol University, the Small and Medium Enterprise Development Bank of Thailand and the National Innovation Agency established Stang Holding as a private company in 2004 to help manage intellectual properties resulting from research and to provide co-investment services.

To date, some examples of their venture capital enterprises include:

International BioService Co. Ltd.

IBS offers services in the study, analysis and testing of drugs, including bio-efficacy tests and pharmaceutical equivalence tests between the existing drug and the prototypical drug.

Aclires Holding Co. Ltd.

The company offers services in clinical research, a significant stage in the R&D process of new drugs or the development of new methods of treatment with existing drugs.

International Drug Development Co. Ltd.

The company is a contract research organization (CRO), offering services in clinical research, specializing in early stage clinical study from the level of Proof of Concept (PoC) to the level of Pre NDA.

For more information, please visit http://stangholding.mahidol.ac.th.

Skilled Labor

To ensure the future development of the biotechnology industry, the National Biotechnology Policy Framework (NBPF) estimates future demand for an additional 500 biotech managers and 10,000 biotech university graduates. Twenty-four of Thailand's universities have the combined annual capacity to supply 800-900 individuals with undergraduate biotechnology degrees, 300-400 Masters recipients and 100 PhDs. BIOTEC is also conducting a regional capacity building program to enhance the skill and availability of human resources for Thailand's biotechnology industry.

Intellectual Property (IP) Protection

Currently there are seven legal acts protecting IP rights in Thailand:

Patent Act B.E. 2522
Copyright Act B.E. 2537
Trademarks Act B.E. 2534
Plant Variety Protection Act B.E. 2542
Protection of Layout-Designs of Integrated Circuits Act B.E. 2543
Trade Secret Act B.E. 2545
Protection of Geographical Indications Act B.E. 2546.

Why Now?

While the world is struggling with economic downturn, there is no better time to look for new pastures. Those who invest now will find their businesses strategically placed to take advantage of the economic upturn when conditions improve. And biotechnology is a business of the future. Thailand is seeking research partners and is actively promoting bio-business as a strategic industry.

mai
Matching Fund Co.,Ltd.

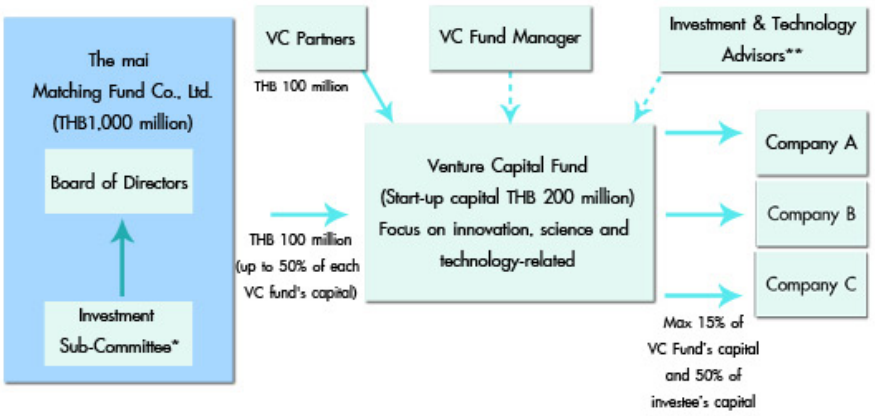
In 2007 the Stock Exchange of Thailand (SET) approved Baht 1 billion to establish the mai Matching Fund Co., Ltd. as a wholly-owned venture capital subsidiary. The fund will indirectly invest in innovative, science & technology related companies via venture capital (VC) funds, focusing on companies deemed important for Thailand's competitiveness. The venture capital fund will target companies with growth potential and the desire to be listed on the Market for Alternative Investment (mai) in the future.

The target industries include food, automotive parts & accessories, software, microchips, textiles, tourism, healthcare and biotechnology. These sectors have been selected for development under the National Science and Technology Strategic Plan (2004-2013). Other industries using science and technology may also be eligible if approved by the Board.

The mai Matching Fund will invest up to 50% of each VC fund's capital base in the form of non-voting preferred shares. The professional fund manager will be independent of mai Matching Fund.

For more information, please contact mai Matching Fund at http://www.mai.or.th.

Investment Scheme



* An Investment Committee will evaluate which VC funds to invest in.
**Investment and technology advisors to consider target companies to invest in.

NATIONAL SCIENCE AND TECHNOLOGY DEVELOPMENT AGENCY (NSTDA)

LEADING THE WAY

Since its establishment in 1992, NSTDA has served as a major base where leading scientists and experts can meet and work on scientific and technological issues of immediate concern to both the national and international communities. The focus of the Agency is to nurture research and development to strengthen Thailand's sustainable competitiveness, complemented by technology transfer and the development of human resources and science and technology infrastructure, with results that have a positive impact on society and the economy. To achieve the goal, NSTDA provides and manages research grant focusing in the following industrial clusters and areas: 1) food and agriculture; 2) medical and health; 3) software, microchip and electronics; 4) automotive; 5) renewable energy; 6) environment; 7) textiles; 8) rural community and the underprivileged; and 9) platform technology which includes basic research.

The Agency encompasses a number of research centers viewed as critical towards developing science and technology in the country. These include the National Nanotechnology Center (NANOTEC), the National Metal and Materials Technology Center (MTEC), the National Center for Genetic Engineering and Biotechnology (BIOTEC), the National Electronics and Computer Technology Center (NECTEC) and the Technology Management Center (TMC).

In its relatively short lifetime, NSTDA has managed to implement and support a wide range of programs and activities that have greatly enhanced the economic and social development of Thailand. These have been carried out through cooperation and networking with more than 30 universities, educational institutions and government agencies, as well as with the business community.

For more information, please visit http://www.nstda.or.th.

Technology Management Center (TMC)

TMC is the commercial arm of NSTDA, helping drive Thai industry, particularly SMEs, to become knowledge-based, and to move up the technology ladder. TMC has particularly focused on facilitating the growth of high-tech industry.

TMC offers a variety of assistance schemes to industry, including financial assistance, facilities assistance and technology assistance. Financial assistance takes the form of research grants; soft loans for research and development, company start-ups, new technology, etc.; co-investment in pioneering or high national impact projects; and tax incentives offered in conjunction with the Revenue Department for R&D projects.

Facilities assistance primarily includes the facilities at the Thailand Science Park, which has land for lease, rental space and incubator space for start-up firms, starting from as small as 10 square meters, as well as extensive equipment and human resources.

TMC offers a variety of technology assistance programs, ranging from information services, training programs, testing and analytical services, contract research, consultancy and matchmaking services, technology licensing and more. The Industrial Technology Assistance Program (ITAP) is one of the most successful programs aimed at helping firms overcome technical obstacles. Various other programs are available from TMC include the Support for Technology Acquisition and Mastery Program (STAMP) and many more.

For more information, please visit http://www.tmc.nstda.or.th.

National Center for Genetic Engineering and Biotechnology (BIOTEC)

As a premier research institute in both Thailand and Asia, BIOTEC operates research units located within the Thailand Science Park, as well as specialized laboratories hosted by various universities, employing over 530 staff, of which 135 are PhD researchers and 240 research assistants and lab technicians. BIOTEC research covers a wide spectrum from agricultural science to biomedical science, biodiversity and environmental science. Apart from research laboratories, BIOTEC activities also include policy research, bio-business, biosafety, an outreach program, training and international relations.

BIOTEC has established multiple laboratories for conducting research and/or providing technical services. Some laboratories act as stand-alone research centers in their own right, while others are collaborative ventures set up jointly with government agencies and universities. This latter arrangement has been instrumental in boosting research competency within these universities. BIOTEC's research units and specialized laboratories conduct basic and applied research covering a wide spectrum from advanced genetics and proteomics to simple solutions for farmers.

BIOTEC income is sourced from government funding and revenues from providing services/commercialization and non-government entities such as international funding agencies and private foundations.

For more information, please visit http://www.biotec.or.th.

AGRICULTURE AND FOOD

MAINTAINING THE LEAD

Thailand is the world leader in the production and export of many agricultural products, including rice, cassava, sugar and rubber. It is the 14th largest agricultural and food exporter in the world (or the 5th largest if all the European countries are considered as a single community). The food and agriculture industry is therefore an important contributor to the economy. However, to maintain its lead and share in the world market, the industry must overcome several challenges including productivity, quality and food safety and one of the biggest challenges facing Thailand is its continued ability to export agricultural commodities to the USA and the EU.

Thailand can differentiate its products from its low cost competitors by establishing an image as producers with high food safety standards. In addition, for the food and agriculture industry to overcome these challenges and remain competitive, it must tap biotechnology to achieve greater productivity and higher quality in production – maintaining Thailand's edge in the global agriculture market.

Under the National Biotechnology Policy Framework (NBPF), Thailand will use biotechnology to enhance its competitiveness in the agriculture and food industries. The goal is to increase the export value of the country's raw and processed agricultural products to 1.2 trillion Baht by the end of this year, which is over 3 times the 2002 export value.

Essentially, the NBPF will place emphasis on applying core technologies such as genomics, plant and animal breeding (by means of molecular breeding) and bioinformatics to accelerate development in agricultural and food production. In the mid-seventies, Thailand was one of the first countries in the region to utilize biotechnology to increase agricultural productivity. This had led to numerous government-supported commercial successes.

Plant Transformation

An early application of this technique in Thailand's agricultural scene was the development of transgenic tomato plants resistant to the tomato yellow leaf curl virus. BIOTEC's Plant Genetic Engineering Unit at Kasetsart University has successfully created tomato plants that carry the coat protein gene of the tomato yellow leaf curl virus, to help control this economically-damaging viral disease. The same approach was taken to develop transgenic papaya and pepper that are resistant to the papaya ringspot virus (PRSV) and transgenic chili that is resistant to the vein-banding mottle virus. Most of these transgenic plants are now being tested in confined conditions in compliance with Thailand's bio-safety guidelines.

Among Thailand's transgenic plant development programs, the most advanced is the one for virus resistant papaya and currently two varieties of transgenic papaya are undergoing food safety assessment.

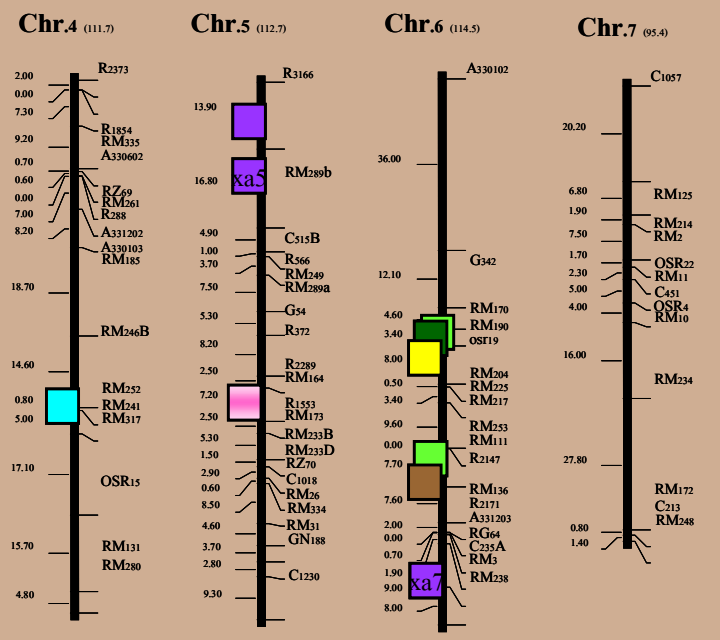
Marker-assisted Selection

In Thailand, marker-assisted selection has been used in breeding programs for tomatoes, to select for plants showing resistance to bacterial wilt as well as nematode, tobacco mosaic virus, fusarium race 2, late blight and powdery mildew. Resistant lines are currently being evaluated in multi-location fields by private companies.

Downy mildew is one of the most destructive diseases found in maize in Thailand. Researchers have been using molecular techniques, such as Simple Sequence Repeat (SSR), to define marker positions that link to the QTLs of the disease, which are then used in marker-assisted selection. Eight novel QTLs for resistance have been found.

Work is ongoing with rice breeding programs focusing on conferring tolerance to submergence and resistance to brown plant hopper for the most important economic rice varieties.

Molecular genetic markers are now being applied in selective breeding programs for commercially important marine species. Species-specific markers found in several marine species are used for identification of correct broodstock and seed species, as well as for quality control of commercial trading of oyster, mud crab and abalone seed. A population-specific RAPD marker found in black tiger shrimp from the Andaman Sea has been used to verify growth and survival performance among different black tiger shrimp stocks in commercial culture ponds.



RICE

Thailand is the leading exporter of rice and is well known for its fragrant or jasmine varieties, popular in many countries. The premium quality variety is known as KDML 105 and Thailand already has introgression lines with submergence tolerance, bacterial leaf blight resistance, leaf blast resistance, brown plant hopper resistance, drought and salt tolerance. Future efforts will look into putting these traits together by gene pyramiding via marker-assisted selection.

Thailand is also a member of the International Collaboration for Sequencing the Rice Genome, focussing on chromosome 9, and made use of this experience and data to enhance the competitiveness of Thai rice. Improving the cooking quality, aroma, nutritional value and response to biotic and abiotic stresses are the top priorities for research.

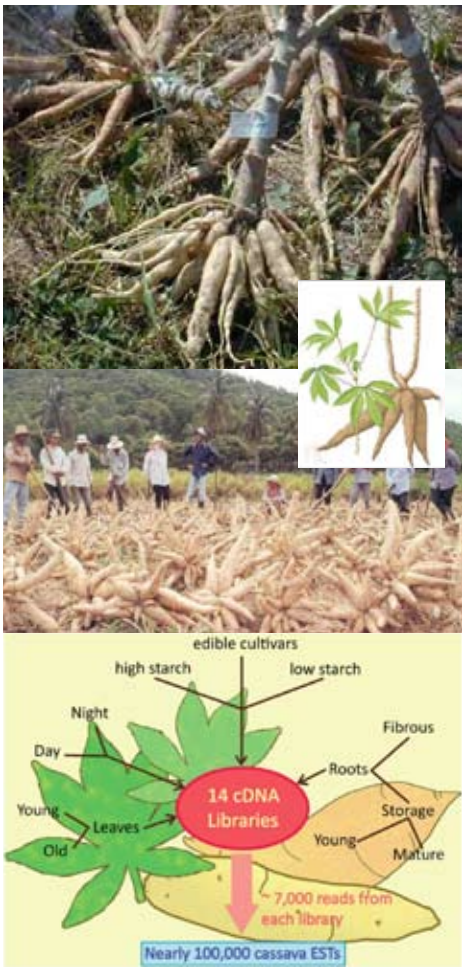
To determine new allelic forms of valuable QTLs, critical mapping populations have been developed from the crossing between KDML 105 and landraces and wild rice. The aim of this particular project is to bring Thailand into the international scientific arena, push state-of-the-art technology into the local research and industry scene, as well as to enhance Thailand's competitive edge in the international rice market.

CASSAVA AND STARCH

Cassava is one of the most important commercial crops in Thailand. It is exported mainly to Europe in the form of chips for animal feed. The starch produced from cassava has wider utilization in both food and non-food applications. Industrial utilization of cassava starch has now expanded from being primarily used in paper, textile and plywood industries to the production of biofuel and biodegradable polymers. There are currently over 70 factories producing around 2 million tons of starch per annum. For the domestic market, the largest proportions of native starch go to the industrial production of food flavor enhancers, such as monosodium glutamate, lactic acid and amino acid production for feed supplement, such as lysine.

The main aim of cassava variety improvement in Thailand is to enhance starch yield. Other selection criteria for variety improvement include early harvest time, starch quality, root shape, white flesh and tolerance to pest and diseases. Improvements achieved through conventional hybridization already include nine new varieties with highly desirable characteristics that have been released for industrial use. Current research focuses on two important aspects of starch biosynthesis in cassava; the sucrose partitioning pathway and the biosynthesis of starch granules in the roots. To gain a better understanding of the starch biosynthesis in cassava, identification and extensive expression analyses are being carried out at the molecular level, looking at the enzymes involved in the starch biosynthesis in different cassava cultivars with varying storage starch levels.

Basic studies of cassava starch structure, as related to its functions, also offer more opportunities for researchers to develop industrial applications using cassava starch. The Cassava and Starch Technology Unit, a specialized BIOTEC laboratory established in 1995 at Kasetsart University, has been investigating the physicochemical properties of cassava. In addition, BIOTEC and the Nara Research Institute of Science and Technology in Japan have been collaborating to establish a cassava EST collection for transcription profiling of the cassava genes. Based on this technology a broad spectrum of genes, with many being novel, involved in starch biosynthesis control can be discovered from these studies.



SUGARCANE

Thailand produces about 73 million tons of sugarcane annually. Strategies for improve productivity include better farm management, irrigation and improved varieties. Each variety has specific characteristics suitable for a particular planting area and environment.

Research on improving sugarcane for food focuses on high biomass (increasing high productivity per unit area), high sugar content (13 CCS), disease resistance, ratooning ability (more than 2 crops), while for energy cane the focus is on high fiber (raw material for electricity) and high sugar content (raw material for ethanol production). For forage cane the focus is on digestibility (soft fiber) and higher nutritional value for animal feed.

Numerous varieties have been collected both domestically and internationally to establish a germplasm base. This includes 1,280 varieties identified by 20 SSR microsatellite markers. Molecular markers have been used for yield improvement, including developing a DNA marker for high sugar content.

Hybrid populations from Phill6607 with high sugar content have been crossed with wild species and used to map the QTL with AFLP and SSR markers. The resultant populations have been used to study ratooning ability, red rot – wilt and smut disease.

BIOTEC has been collaborating with Mitrphol Research Ltd. and Innova Biotechnology to develop a white leaf disease test kit (lateral flow IC). The test kits are used for detection of the white leaf disease from the parent clone before mass production by tissue culture technology and for detection in the seedling stock before distribution to growers.

SEED

The seed industry is considered to be an essential driving force in the modernization of Thailand's agriculture sector and modernization is focused on greater value creation of existing agricultural commodities, where Thailand is already a world leader in production. Due to a favorable climate and fertile farmland, Thailand is currently the seed production and manufacturing base for many international seed conglomerates. In 2006, there were over 100 local and foreign seed companies in operation, employing more than 28,000 families and contributing over US$420 million (not including local demand of over US$300 million) to the Thai economy.

To move the seed industry to the next level, the strategic plan for the development of the industry will focus on cucumber, chili, tomato and corn. This is because of Thailand's existing advantages in these areas due to its access to germplasm, its access to variety improvement technologies, its production capability, its sizeable local market base and even larger export market base, as well as advancements in biotechnology research and development.

BIOLOGICAL CONTROL

In addition to the obvious dangers from overuse of pesticides, the growing popularity of organic produce among consumers around the world represents an opportunity for Thai farmers, who are well positioned to supply fresh organic produce, especially fruit and vegetables, internationally.

While field application is still limited, some successful bio-control programs include:

- UNIGREEN UN-1 (*Trichoderma harzianum*) was approved by the Department of Agriculture in 1996, as the first registered bio-fungicide in Thailand.
- Support from BIOTEC and the Thailand Research Fund has resulted in the commercialization of *Trichoderma*, to control *Sclerotim rolfsii Sacc.*
- Support from BIOTEC and the Thailand Research Fund has also resulted in the commercialization of *Chaetomium,* to control soil fungi such as *Phytophthora*.
- In 2005, Agromed successfully commercialized a product derived from the fungi, *Paecilomyces lilacinus*, to control naematodes.
- BIOTEC and the Department of Agriculture have joined hands to set up a pilot-scale production facility for the production of NPV (nuclear polyhedrosis virus). NPV is widely used to control the *Spodoptera* moth in the production of grapes and asparagus.

Pilot plant production facility for NPV located at Thailand Science Park

SHRIMP

Thailand is a leader in cultivated shrimp production and it has gained a competitive advantage through higher farm productivity and better disease control. Major export markets for Thai shrimp are the USA and Japan.

Domestication of black tiger shrimp is critical to help overcome the problems arising from the use of wild shrimp and domesticated stocks. It also allows for the selection of important traits, such as the fast-growing or disease-resistance strains in this species. Raising domesticated specific pathogen-free (SPF) black tiger shrimp broodstock is one of the main research priorities and it involves both the government and the private sector.

To gain further insight into molecular aspects governing reproductive processes and immune systems of black tiger prawn for future functional genomic studies, a large-scale expressed sequence tag (EST) sequencing project has been undertaken. cDNA libraries were constructed from different tissues, including the eyestalk, hepatopancreas, haematopoietic tissue, haemocyte, lymphoid organ and ovary of shrimps reared under normal or stress conditions.

Shrimp have an efficient innate immune system to defend against invading foreign materials and this enables them to live in an environment rich in bacteria and viruses. Research in Thailand has thus been directed towards the identification and characterization of immune effectors, the development of assays to evaluate and monitor the immune state of shrimp and the selection of disease-resistant shrimp.

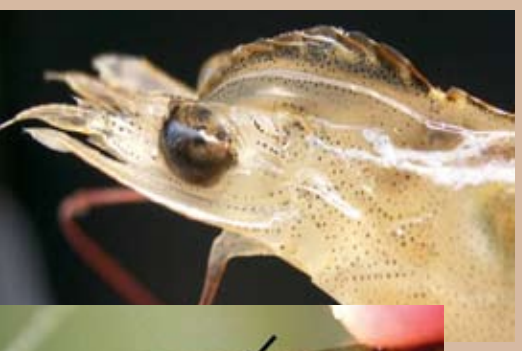
A Shrimp Success Story

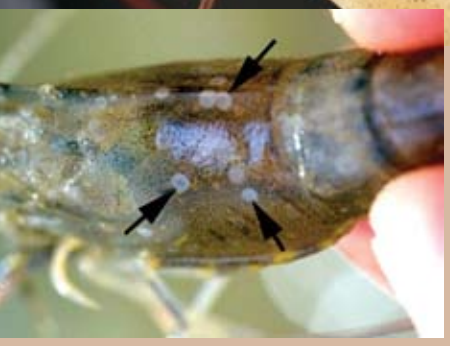
Viruses affecting shrimp is an international p
out in China in 1993, the effects were devast
incident prompted Thailand to immediately begi
outbreaks had yet to occur in the country, now
world. Research was undertaken to investigate
to develop effective diagnostic probes.

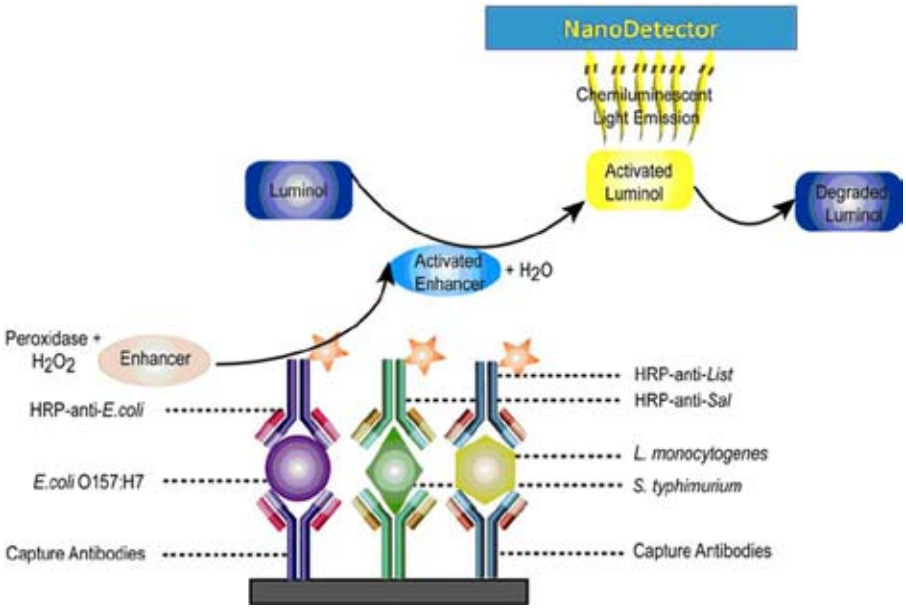
In 2000 shrimp production in Ecuador dropped fr
the drastic reduction in shrimp production elsew
and China, due to outbreaks of WSSV, shrimp
tons in the year 2000, compared to 243,000 ar
The rise in production in Thailand during the t
prevention scheme that was put in place. The s
effective application of diagnostic kits to screen
before major outbreaks. Investment in R&D ir
returns to the shrimp farmers and the Thai eco

roblem. When White Spot (WSSV) first broke tating, with production dropping by 77%. This in work on combating the problem, even though regarded as the largest shrimp exporter in the the biology and the source of the virus, in order

om 144,000 tons in 1998 to 45,000 tons. Despite where in the world, particularly in South America production in Thailand rose to 280,000 metric d 230,000 tons in 1998 and 1999, respectively. ime of WSSV infection can be attributed to the success of this scheme is in turn credited to the stocking fry for early detection of the infection this area by Thailand has yielded substantial nomy in general.







Microarray Technology for Agriculture and Food Application

Microarray technology allows high-throughput screening and analysis. BIOTEC Microarray Laboratory is equipped with technologies to fabricate array chips in-house as well as applying them in various aspects of research and development. To understand fundamental biology of black tiger shrimp (*Penaeus monodon*), the first version of cDNA microarray has been constructed to study the reproduction and nutrigenomics of this economically important animal.

The second area of interest is to develop diagnostic kits by interfacing microarray technology with biological molecules such as antibodies. A prototype of antibody array has been developed to simultaneously detect multiple food-borne pathogens (*E. coli* O157:H7 *Salmonella* spp. and *Listeria monocytogenes*) using a chemiluminescent detector, NanoDetector. This system is based on chemiluminescent immunoassay similar to mini sandwich Enzyme-Linked Immunosorbent Assay (ELISA). Each slide can accurately detect three pathogens at the same time. The sensitivity and specificity are equivalent to those of conventional ELISA. However, the assay time required for this system can be reduced from 5 hrs to only little over 1 hr without affecting sensitivity and accuracy of the system. Equally as sensitive as ELISA, the antibody array uses very small amounts of the capture and HRP-antibodies. The advantages of the antibody array make this technology more appealing for commercialization. A higher-throughput system using a 96-well format using a fluorescent detector is also being developed to lower the cost of antibody even more.

MEDICINE AND HEALTHCARE

MEDICAL HUB OF ASIA

Thailand four hundred hospitals offering most advanced treatments by internationally trained medical staff. The country boasts the largest hospital in Southeast Asia and the first ever to receive ISO 9001 certification, as well as having the first hospital in Asia to be granted Joint Commission International Accreditation (JCIA).

In 2008, the number of foreign medical tourists arriving in Thailand reached 1.5 million and a target has been set for 2 million by the year 2010. In the same year the Thai Government declared a five-year strategic plan to develop the sector to become "The Center of Excellent Health of Asia".

Since 2005, the market in Thailand for medical equipment and supplies has grown at a rate of 20% annually. Within the Asia and Pacific region, the medical equipment and supplies market is projected to reach as high as US$43 billion within the next three years. Approximately 87% of the medical device equipment and accessories are imported.

Thailand is taking the lead in the manufacturer of diagnostic kits, orthopedic products and other disposable devices. According to the Rubber Research Institute of Thailand, the domestic demand of rubber gloves in 2006 was for 52,312 tons. Export of rubber gloves totals US$ 78 million annually.

Research

Most of the major hospitals in Thailand, especially the university hospitals are active in research. In addition there are a number of specialist research centers.

The National Science and Technology Development Agency (NSTDA) provides an umbrella for a collection of these centers under their medical and public health cluster. In addition, NSTDA also facilitates partnering for the cluster with an important international network that currently includes:

- Emory Vaccine Center, Emory University, USA
- St. Jude Children's Research Hospital, USA
- Centers for Disease Control and Prevention (US-CDC), USA
- International Development Research Center, CANADA
- Pasteur Institute, France
- Imperial College London, UK
- Chinese Academy of Sciences (CAS), China
- Kunming Academy of Botany, China
- Institute of Biotechnology, Vietnam

For the next three years, the cluster will focus on R&D that includes:

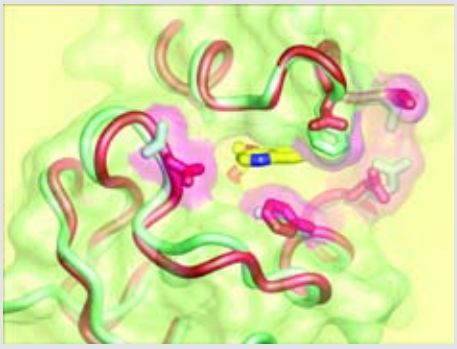
- dengue vaccine development.
- research and development on rapid prototyping model for body repair, reconstruction and rehabilitation.
- basic science studies in preparation for using stem cells and induced-pluripotent stem cells, personalized medicine and genomics medicine.
- standardization of the national health information system.
- development of diagnostics kits/ reagents for emerging and re-emerging infectious disease.

A further focus for the cluster is to develop medical products that will help reduce the current reliance on expensive imported products and to increase the level of Thai exports. The development of medicine and public health is fundamental to the development of other biotechnology industries.

Drug Target Research

The levels of antibiotic resistance of some medically important microbes have reached an alarming level, exemplified by the emergence of extremely drug-resistant tuberculosis as well as drug-resistant malaria. Most antibiotics bind specifically to target proteins and disrupt their functions, leading to bacterial cell death or growth arrest. Current antibiotic targets include only a few dozen proteins in contrast to the hundreds of possible targets.

A team of BIOTEC researchers have focused on identifying anti-malarial targets and developing test methods based on folate metabolism. This pathway provides two targets for current anti-malarials: dihydrofolate reductase (DHFR) and dihydropteroate synthase (DHPS). Other enzymes of interest as drug targets in the pathway include thymidylate synthase, an enzyme naturally fused with DHFR in the malarial parasites, serine hydroxymethyltransferase, methylene tetrahydrofolate dehydrogenase and methionine synthase. The success of this research is exemplified by the recent issue of a US patent on pyrimidine derivatives that inhibit the plasmodium enzyme.



The active site of malarial DHFR (green) aligned with that of the human enzyme (red). The inhibitor P113 (yellow) is bound in the sites. A main objective of the research, with support from MMV, is to design inhibitors with selectivity for the malarial enzume, so as to develop them as antimalarial candidates.

P. falciparum DHFR-TS
(Nature Struct. Biol. 2003, 10, 357-365)

cGMP Pilot Plant for Biopharmaceuticals

In 2007, King Mongkut's University of Technology Thonburi (KMUTT) Industrial Park and BIOTEC decided to collaborate to set-up Thailand's first government-supported cGMP facility for scale-up study and production of recombinant proteins for clinical trials, as well as for training manpower. It is of critical importance to position this new cGMP Pilot Plant as a linkage from the laboratories to real industrial applications in order to maximize the profit of local research in the field of microbial production of biopharmaceuticals. KMUTT's Industrial Park is strategically located in the heart of one of Bangkok's major industrial areas. This new 3-storey facility with the cGMP Bioprocess facility established on the first floor will be the center point of the Industrial Park Center supporting and promoting companies interested in advanced biotechnology and products through collaborative R&D, contract R&D and contract manufacturing. This pilot plant is scheduled to be ready to commence operations in 2010.

The cGMP Bioprocess facility is composed of two suites each dedicated exclusively for microbial and cell culture fermentation systems of up to 400L and 100L bioreactors, respectively, which are each supported by separation and purification processes. The Plant has been designed to comply with global regulatory guidelines and standards: US FDA, EMEA and Thai FDA. The services offered will range from scale-up and bioprocess development, biologics/biosimilars production for preclinical and clinical trials phases I and II, process optimization for manufacturing processes, and training on cGMP, GLP, Biosafety, Regulatory Compliance, SOP, QA, upstream and downstream processing. The Plant will give emphasis to creating a strong network through the value chain of biopharmaceutical manufacturing, through collaboration with other NSTDA agencies, the Government Pharmaceutical Organization (GPO), Mahidol University and others. A multidisciplinary team of scientists and engineers will ensure that appropriate process development meets customer requirements with affordable cost-effective services.

BIOTEC-Novartis Drug Discovery Partnership

The National Center for Genetic Engineering and Biotechnology (BIOTEC) and Novartis AG first formed a partnership in 2005.

The partnership is based on the complementary expertise of both parties. BIOTEC's expertise lies in the knowledge of certain microorganisms, ranging from collection, identification, preservation to culturing conditions and in the isolation and preliminary characterization of pure natural compounds from such microorganisms, whilst Novartis has expertise in the discovery, characterization, development and worldwide commercialization of compounds derived from both synthetic and natural-product sources. The partnership aims to find potential use of microorganisms and natural compounds derived from microorganisms, as sources for innovative medicines.

During the first phase alone, more than 2,500 microbial isolates and 70 pure compounds were investigated. Many of the microbial strains have proven their ability to produce new compounds. The pure compounds and extracts from the microbial strains continue to be evaluated against novel drug targets from all disease areas of the Novartis research portfolio, such as infectious and cardiovascular diseases, oncology, or immunology.

Capacity building is an important element of the partnership and has also enabled BIOTEC to automate and improve its extraction and chemical screening systems. Expertise in taxonomy and isolation of certain types of microorganisms acquired during the Partnership also enabled BIOTEC to discover 2,000 more strains. These strains are considered to be assets of Thailand and are now maintained at the BIOTEC Culture Collection where they are available for other research programs.

Encouraging results have led both parties to extend their partnership, in July 2008, for a further three years.

BIODIVERSITY AND BIORESOURCE UTILIZATION

STRENGTH IN DIVERSITY

Due to its geographical position in the tropics and the climatic variations between north and south, Thailand is a country of high biological diversity reflected by the number of species. The total number is potentially very large with the country being at the junction of several natural “highways” linking south and north and thereon westwards.

It is estimated that only 20% of Thailand’s flora, for example, has been well documented. Given that the country hosts between 7-10% of the world’s biological resources, the potential for new discoveries is significant, particularly in the area of plants, fungi and microorganisms. BIOTEC has embarked on an ambitious survey campaign to measure these resources and to develop the human resource skills base to buildup more accurate inventories. The focus for research is on fungi and microorganisms as these offer the highest potential for discovering new bioactive compounds.

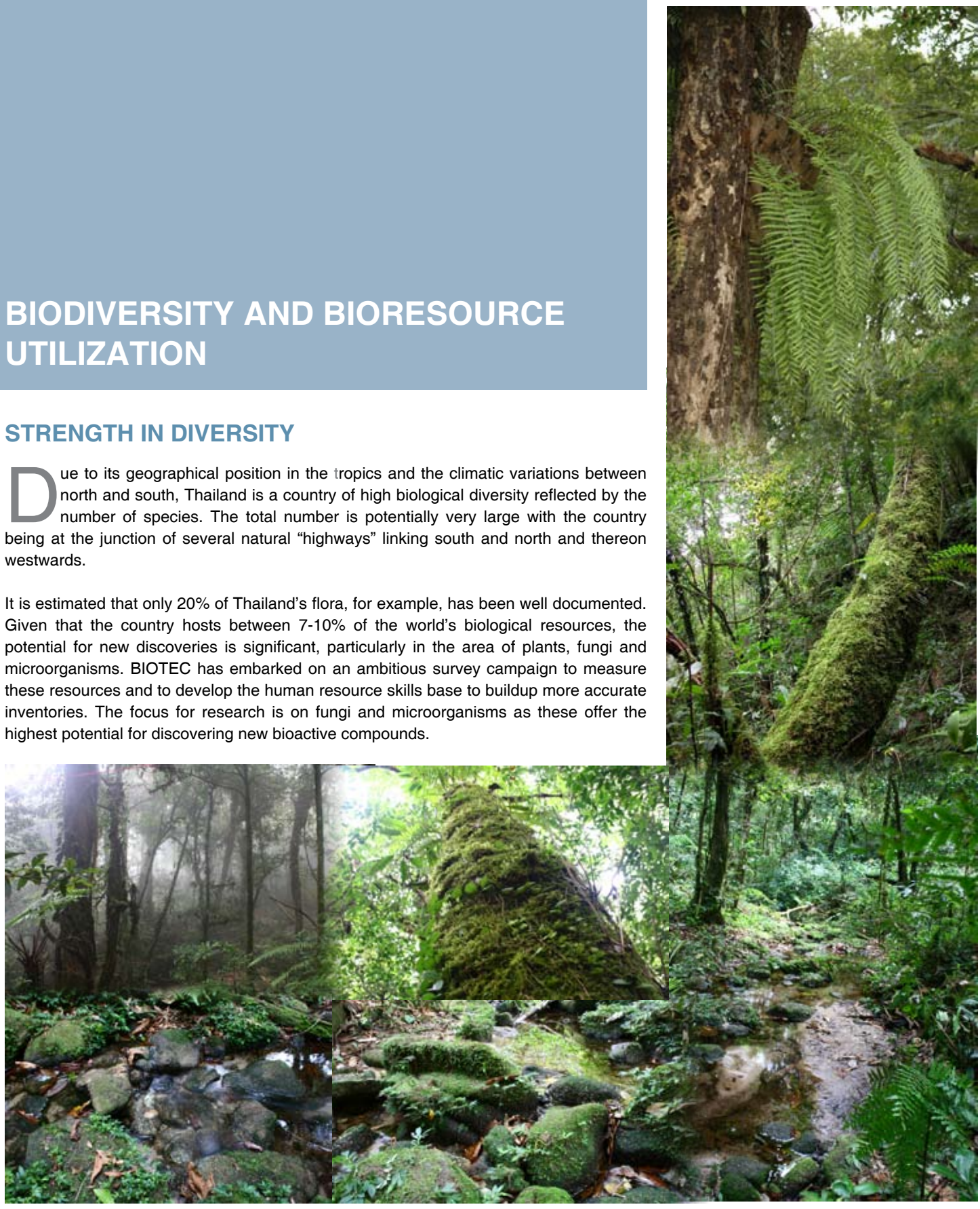


Photo by The Biodiversity Research and Training Program (BRT)

Collection

Collections of microorganisms are usually maintained in the form of a culture. In Thailand many of these are working cultures maintained by individual scientists. The documentation accompanying the culture is an essential element for further study. In addition to being the driving force behind the establishment of a national collection and associated network, BIOTEC has developed a Microbial Information Management System (MIMS) to serve the needs for microbial biodiversity preservation and utilization. The system generates species inventories, culture catalogues and species distribution maps, in addition to producing species summaries, locality summaries, fermentation and summaries for screening of bioactive compounds. Thailand is also an active partner in the UNEP/UNESCO Microbial Resource Center for South East Asia.

The Thailand Network on Culture Collection currently includes the following agencies:

- BIOTEC Culture Collection (BCC) - Collection of Fungi and Yeasts
- Department of Medical Science - Collection of Human Pathogenic Microorganisms
- Department of Agriculture - Collection of Plant Pathogenic Microorganisms
- Thailand Institute of Scientific and Technological Research - Collection of Waste Recycling and Industrial Important Microorganisms

Number of microorganisms preserved at BCC (as of December 2008)

Type	Total
Algae	201
Bacteria	5,888
Fungi	22,940
Yeasts	2,092
Total	31,121

Freshwater Fungi | Marine and Mangrove Fungi | Insect Pathgenic Fungi

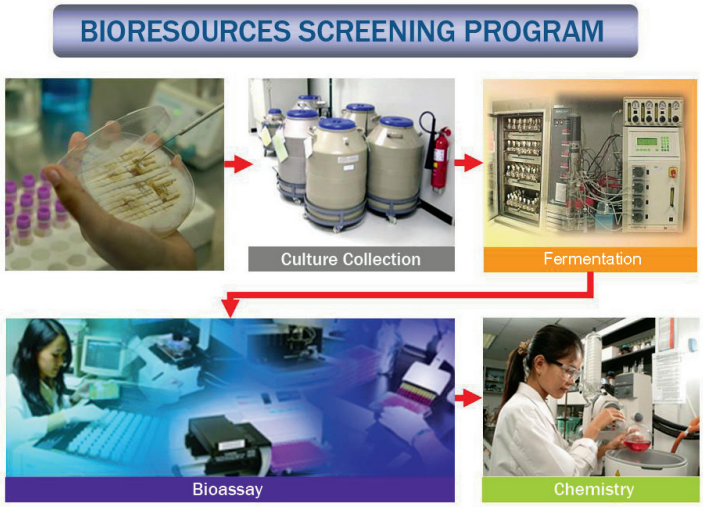
The Hidden Potential of Fungi

It is estimated that perhaps as little as 1% of Thai fungi have been described to date. Entomopathogenic fungi alone offer tremendous potential as a source of novel metabolites exhibiting various biological activities ranging from activity against malarial parasites, fungi, virus, mycobacteria and tumor cell lines.

Research centers throughout the country are active in unraveling the mysteries of these biological resources. The Mycology Laboratory at BIOTEC is working on insect pathogenic fungi, freshwater aquatic lignicolous fungi, seed fungi, basidiomycetes and marine fungi. At Burapha University, marine fungi are under investigation with particular interest in omega 3 polyunsaturated fatty acids and bioactive compounds from mangrove fungi. Chiang Mai University in the north has a research group investigating endophytic fungi from a variety of trees and shrubs, including their ability to produce various enzymes and bioactive compounds. The diversity of macro fungi from soil is also under investigation and active study of endophytes from teak is also being undertaken. Soil fungi also form the major focus for research at Kasetsart University, while projects on endophytes and pathogenic fungi of orchids, rhizosphere fungi and coprophilous are also in progress. KMUTT conducts a number of mycological projects, including the biodiversity of macrofungi, qualitative and quantitative estimation of lignocellulose breakdown by Xylariaceous fungi and basidiomycetes, ultrastructure of Coelomycetes, morphology, physiology and fatty acid profiles of *Aschersonia* species for identification of related taxa, molecular biology of *Aspergillus oryzae* emphasizing heterologous gene expression, alkaline protease production from *A. oryzae* and identification of mychorrizal fungi using PCR techniques. Programs are also ongoing at Chulalongkorn, Prince of Songkla, Ramkhamhaeng and Suranaree Universities, as well as the Royal Forest Department.

Screening

Natural products, particularly plants, have traditionally provided a rich source of chemical diversity in the search for new biologically active molecules, but it is only over the last 50 years that microorganisms have been seriously exploited as a source of antibiotics and pharmaceuticals. However, a significant proportion of prescription medicines are microbially derived and include some of the top selling drugs used as antibiotics, serum cholesterol lowering agents and as immunosuppressants.



In order to exploit the full extent of the chemical diversity of microbial secondary metabolites, it is advantageous to screen very large numbers of samples. A screening strategy and technology should be rapid and effective to detect molecules at low concentrations in which is often a complex mixture. However, screening activities are expensive and risky. To potentially utilize bioresources and to support the work on bioactive compounds in Thailand, BIOTEC established a Bioassay Research Facility, incorporating Fermentation, Bioassay and Natural Products Chemistry laboratories.

The research facility also offers services in bioactive compound screening to both the private and public sector. Scientists in the laboratory are constantly modifying existing assays in order to enhance accuracy and sensitivity in addition to developing new assays. Currently, the laboratory offers assays to detect samples with the following properties:

- Anti-cancer
- Anti-fungal (*Candida albicans*)
- Anti-herpes simplex virus type-I
- Anti-inflammatory, the development of rapid throughput screening for anti-inflammatory compounds.

The facility has two unique murine cell lines capable of identifying the selective inhibition of the COX-2 enzyme over COX-1 and it is currently developing a solid phase RIA assay to measure prostaglandins, suitable for rapid screening due to its lower cost compared with commercial kits.

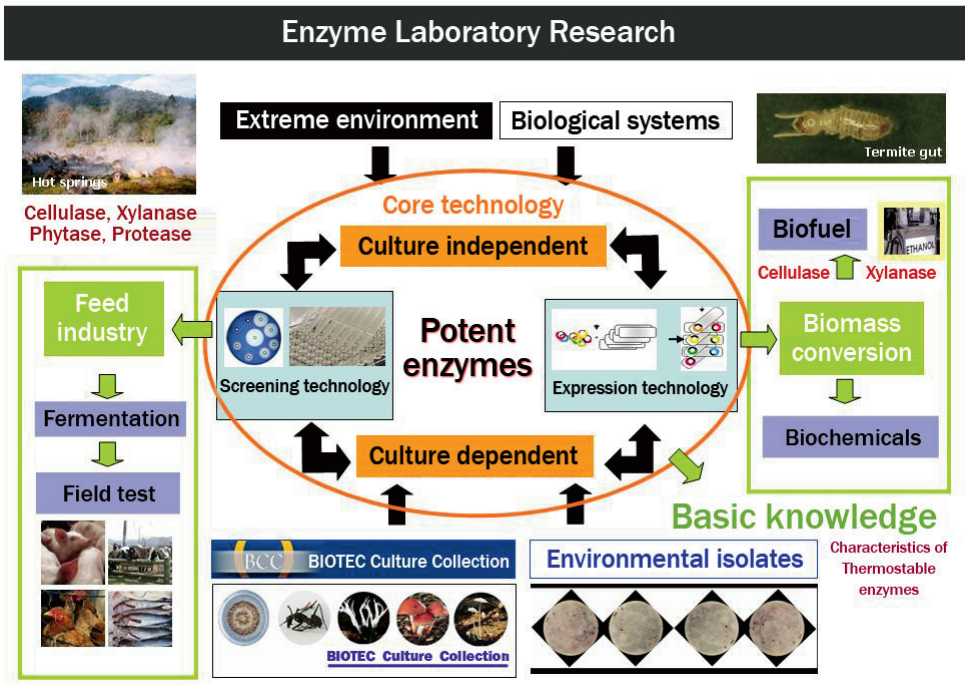
- Anti-tuberculosis
- Anti-malaria
- Anti-metatstasis
- Two cytotoxicity testing methods

Samples that test positive in the anti-cancer assay can further be tested to identify the mechanisms involved using the following tests.

- Anti-ras
- Anti-topoisomerase
- Anti-mitotic cell division
- Anti-telomerase

Since the founding of the program in 1996, the bioassay scientists have investigated over 40,000 samples, both crude extracts and pure compounds from plants and microorganisms with some positive results.

Microorganisms also provide a good source for enzymes. Research at the BIOTEC Enzyme Technology Laboratory focuses on enzymes currently utilized by the major industries in the country. Work in the laboratory includes all aspects of enzyme biotechnology from screening of enzymes from microbial isolates and from metagenomic libraries, gene isolation, enzyme production in wild-type microbes and recombinant systems, to development of enzymatic processes in industry. Current interest centers around lignocellulose degrading enzymes, amylolytic enzymes, lipases/esterases and phytases as well as some specialty enzymes of biotechnological value. Enzymes capable of working under extreme conditions applicable for industrial processes are of special interest.



BIOTEC-Shiseido Research Collaboration

Shiseido joined hands with BIOTEC in 2004 in a joint search for active ingredients with potential for application in cosmetics. In 2008, this collaboration resulted in a joint application for a patent in Japan and Thailand.

In 2006, Shiseido opened their Southeast Asian Research Center located in the incubation unit at the Thailand Science Park. The establishment of the Center helps fostering joint research projects between Shiseido and BIOTEC and this active collaboration includes research on microbial diversity on facial skin.

Joint research has to date identified potential activities in *in-vitro* tests in six plant species:

- *Cinnamomum ilicioides* possessing whitening effect, anti-aging effect, anti-skin roughness activity.
- *Lepisanthes fruticosa*: anti-aging and slimming effects.
- *Fagraea fragrans*: anti-aging and anti-skin roughness effects.
- *Pterocarpus indicus*: anti-aging effect.
- *Boesenbergia regalis*: whitening and anti-aging effects.
- *Aquilaria crassna*: whitening and anti-aging effects.

Shiseido and BIOTEC filed a patent of this discovery in both Japan and Thailand in June 2008. Both parties are in the process of developing more projects that can make best use of the expertise of both sides.

Press conference annoucing joint patent application held in July 2008 in Bangkok, Thailand

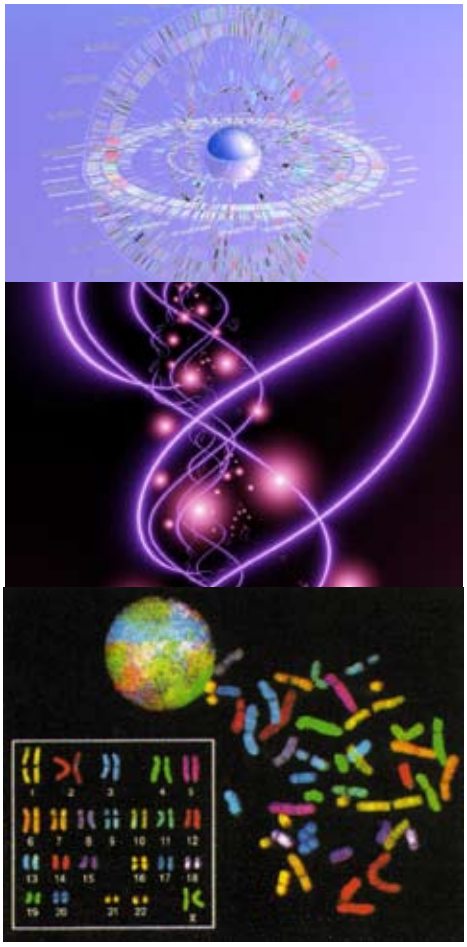
Thailand is fortunate in having some remaining areas of peat swamp forest as these provide a wealth of biological resources not usually encountered elsewhere. They also offer a unique habitat for the study of fungi which enjoy the moist environment. In order to isolate enzymes or metabolic pathways of interest from the uncultured microbial peat swamp community, DNA technology is used to construct metagenomic libraries, representing the total genome of microorganisms from this particular environment. This approach has proved successful for identifying industrially important enzymes, including novel cellulases, xylanases and lipases.

GENOME TECHNOLOGY

INVESTMENT IN THE LIFE SCIENCES

With a wealth of biodiversity, a long tradition of agriculture-based industries and an established medical and biotechnological research and development community, Thailand has become an attractive location for life sciences investment. The large amount of data generated in many areas of life sciences requires visualization, management and analysis, principally through bioinformatics. To ensure success, emphasis has been given to establishing core technologies, such as genomics and bioinformatics, to boost development of agriculture, food processing and biomedical research.

Thailand has not lagged behind in bioinformatics research activity and recognizes the importance of bioinformatics through increased policy awareness, human resources development and increased research activity involving genomic-scale data generation and computational analyses. Many applications of genomics and bioinformatics to biomedical research and development in Thailand have progressed substantially during the past few years, leading to successful applications in some specific local areas. However, the applications to other important areas, such as agriculture, are hampered by the limited availability of genomic sequence data and the lack of necessary biochemical/physiological information. With the advent of more and more genomic information in public databases, the research community is striving to adopt comparative genomics to obtain information of direct relevance to the country's health and industrial needs.



Whole genome sequencing

Burkholderia pseudomallei, the causative bacterium of melioidosis, is the first organism to be whole-genome sequenced by Thai scientists. This gram-negative bacterium is a soil saprophyte in melioidosis endemic areas, particularly Southeast Asia. It is responsible for 20% of acquired septicemia cases in northeastern Thailand, with an approximately 50% fatality rate. In 1998, the 7.25 Mb genome of *B. pseudomallei* K96243 was sequenced by a research team at the Wellcome Trust Sanger Institute, with significant contribution from Mahidol University.

A Thai research team participating in the International Rice Genomic Sequencing Project (IRGSP) sequenced two million base pairs from rice (*Oryza sativa* spp. japonica) Chromosome 9, an activity that has fostered the ability of Thai researchers to obtain and utilize large amounts of genomic information.

The dramatic decrease of the DNA sequencing cost over the past few years has allowed researchers to employ the technology to sequence small genomes of organisms important for local research questions. Avian influenza was inevitably chosen due to its impact on Thailand and the rest of the world and to help solve the recent dispute regarding the sharing of the viral samples between the affected developing and developed countries. The sequence information is important for evaluating control measures, such as vaccines or drugs and for monitoring the genetic changes of the circulating avian influenza virus. The information gained could also answer basic and epidemiological questions and trace spreading pathways of the virus.

At the same time, other viruses, such as dengue and viruses of agricultural importance have also been sequenced. Such information provides insight into the evolution of these viruses and pathophysiological understanding of infectious diseases. For example, the genomic sequences of dengue virus type I collected over a 30 year period revealed the associations between genetic diversity and increase in the serotype prevalence, and decline in serotype prevalence with clade replacement. The experience gained from

working with these viruses allows Thailand to effectively utilize genomic sequencing to cope with future emerging viruses.

Thai researchers are also active in SNP discovery and the results to date may help to locate disease-predisposing genes in the Thai population. With support from the United States National Institutes of Health and collaboration with Boston University, high-throughput genotyping studies have been conducted to assess genome-wide SNP allele frequencies of the Thai population from various disease-association studies. The SNPs associated with disease severity have been identified and are being verified. Allele frequencies across a large number of known SNPs were also obtained, which may be useful for other research studies.

Expressed sequence tags (ESTs) are studied to identify genes from agriculturally important organisms, many genomes of which are still uncharacterized. Currently, more than 40,000 ESTs of the black tiger shrimp have been sequenced and more than 10,000 unique gene fragments have been identified. BIOTEC and the Nara Institute of Science and Technology in Japan have collaborated in sequencing approximately 100,000 ESTs from 12 leaf and root libraries of cassava. The sequences will be useful for comparison with Arabidopsis, a dicotyledonous species related to cassava.

In addition to using proteomics in biomedical studies, 2-D gel protein electrophoresis is an established experimental tool in several Thai laboratories and has been used to identify plant and animal proteins expressed in various conditions, including cassava, peanut, shrimp and microorganisms such as *Bacillus*, *Spirulina* and malarial parasites.

Microarray and systems biology is a widely used method for studying gene expression by measuring mRNA abundance by micro- or macroarray hybridization. This method has been used by Thai researchers to study drug mechanisms in tuberculosis, pathogenesis of dengue infections, nasopharyngeal carcinoma and cholangiocarcinoma. Methods for analysis of these data have also been developed.

As the cost of genomic research decreases and more whole genome-scale research projects are completed, many researchers in Thailand have adopted various computational biological methods to analyze the large amounts of genomic data to generate biological hypotheses, which can be subsequently validated by "wet" laboratory experiments. The identification and application of DNA repeats have been used to identify candidate SSRs from cassava, sugarcane, peanut, oil palm, soybean and rubber trees. It is anticipated that these and many more SSR markers will be useful for selective breeding programs.

Early Thai research efforts led to the discovery of variable number tandem repeats (VNTR) in the genome of tuberculosis, which were later shown to be useful markers for epidemiological studies. Tandem repeats have also been found in many bacterial species, including *Escherichia coli, Salmonella, Shigella, Vibrio cholerae, Leptospira* and non-tuberculous mycobacteria. The usefulness of such repeats for epidemiological studies is being further evaluated. For potential drug candidates, a combined docking and neural network approach has been developed to screen anti-HIV-1 inhibitors for two targets, HIV-1 reverse transcriptase and HIV-1 protease.

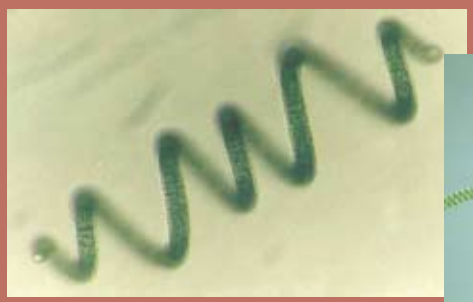
Spirulina

Spirulina platensis is a blue-green algae or cyanobacterium that is industrially important throughout the world, particularly for its use in food and for producing industrially important high value compounds. With over 60% of all digestible vegetable protein, it is the highest protein food available in the world. This unique microorganism also has the highest concentration of beta-carotene, vitamin B-12, iron, trace minerals including the rare essential fatty acid, GLA. In addition, *Spirulina* is also rich in unique phytonutrients such as phycocyanin, polysaccharides and sulfolipids, that have the potential to enhance the immune system, possibly by reducing the risks of infection, cancer and autoimmune diseases.

Currently, the US leads in *Spirulina* global production followed by China, Thailand and India.

Scientists in Thailand have been experimenting with *Spirulina* for quite some time and this resulted in a number of companies entering commercial operation. In 2005, a bold proposal was put forward to try and crack the *Spirulina* genetic code and aim for complete sequencing of the microorganisms' genome. Less than four years later, a consortium of universities, led by KMUTT and with BIOTEC support, were successful, placing Thailand in that exclusive club of only ten nations in the world that have successfully sequenced a genome.

The results of this work will lead to numerous benefits in agriculture, shrimp farming, animal husbandry and healthcare. The milestone success has already encouraged Thai scientists to consider embarking on even more ambitious projects, including plants, and it has demonstrated quite clearly the value of teamwork and investing in genomic research.



BIOENERGY

THE ROLE OF BIOTECHNOLOGY

Thailand has adopted a multiple approach to bioenergy. This involves research on improving the energy yield of plants already known to have high bioenergy potential; it involves exploring new potential sources, such as algae, and it involves applying biotechnology to turn waste streams into energy. The country has been particularly successful in developing both industrial biogas and ethanol. Some of the major sources of available energy crops used in Thailand are sugarcane, molasses, cassava and oil palm. One major challenge Thailand is now facing is how to increase these energy crop yields per area using sound science, technology and management instead of increasing the growing area, which is clearly limited. Such yields must also be increased without adversely affecting the demand for food. This challenge must be met, along with increasing the efficiency of the bio-fuel production process itself.

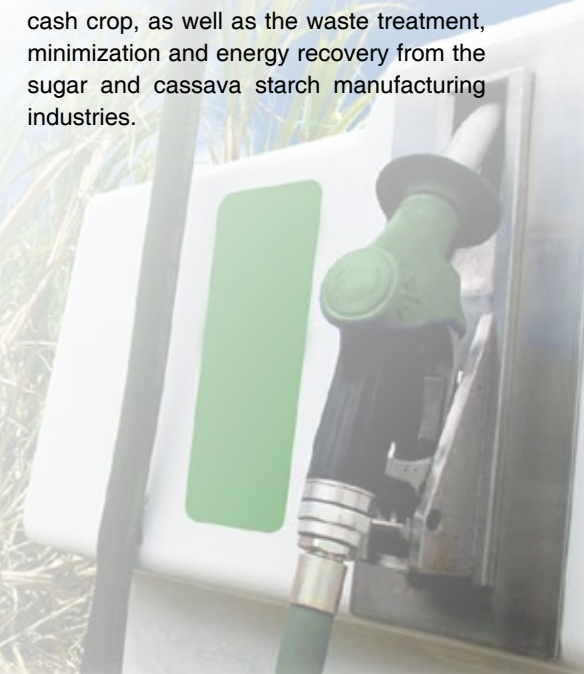
Bioethanol

The ethanol production process from cassava includes conversion of starch to sugar by saccharification and fermentation of sugar to produce ethanol. In a new process, saccharifcation and fermentation take place at the same time, called simultaneous saccharification and fermentation (SSF). This newer method can reduce processing time and energy consumption significantly. The quality of ethanol must comply with regulations issued by the Department of Energy Business to assure the quality of bio-ethanol used in gasohol, a blend of petroleum oil with anhydrous ethanol for vehicle use.

Ethanol production generates solid wastes and wastewater. Solid wastes in the form of thick slop generated from the production line can be utilized for biogas production. It is estimated that for every liter of ethanol produced, approximately 12-20 liters of wastewater is also produced and this is also a potential source for biogas production. 1 liter of ethanol generates 0.35 cubic meters of biogas and this is mostly used in the ethanol plant itself to meet their thermal energy needs for the boilers.

There are several reasons to explain why cassava is considered one of the best raw materials for ethanol production. Firstly, it is an all-year-round crop from plantation to harvest, which is crucial when land use is competitive between cassava and other crops. Secondly, the Ministry of Agriculture has announced a national program to increase the average yield of fresh roots to 30 tons/hectare by promoting high-yield varieties, managing irrigation systems and fertilizers, along with good harvest practice. Thirdly, cassava requires low inputs for planting and harvesting, including investment costs and energy. Utilization of cassava as the raw material for bio-ethanol production needs to be well-managed so that it will not adversely interfere with other industries.

The quantity and raw material cost are major attributes in achieving the Thai Government's target of producing 2.4 million liters of bio-ethanol a day by the year 2011. In the case of bio-ethanol production, the allocation and utilization of feedstock is critical. An increase in sugarcane and cassava productivity is crucial in the long-term for the development of the ethanol industry. The industry provides both economical benefits as well as environmental benefits in terms of the value-addition to cassava as an alternative cash crop, as well as the waste treatment, minimization and energy recovery from the sugar and cassava starch manufacturing industries.



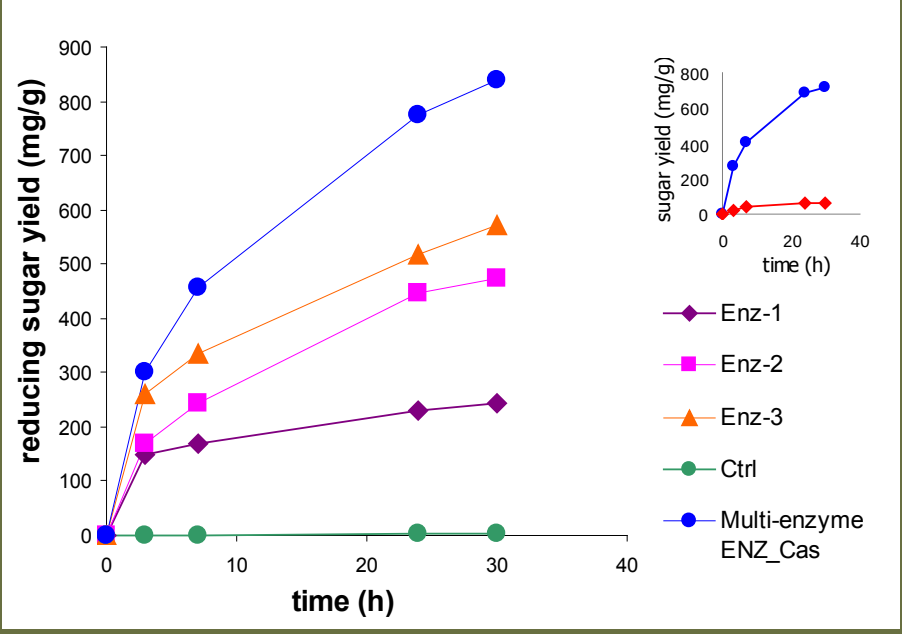
Multi-enzyme for Non-thermal Saccharification of Cassava Feedstock

The Enzyme Technology Laboratory at BIOTEC have been pursing new technology for the development of a cost-effective bioprocess for the production of value-added products from different cassava feedstock in order to maximize the use of this potential starting material for biofuels and chemicals.

In general, two approaches are used for saccharification of starch-based feedstock. Acid hydrolysis is one common approach. However, this process is performed at high temperature with relatively concentrated acid, which leads to the formation of dehydration products and thus reduction in fermentable sugar yield. The enzymatic process is considered a more environmentally friendly approach and has been widely used for saccharification of cassava feedstock. However, the conventional enzymatic hydrolysis of this feedstock is energy-intensive due to the high-temperature gelatinisation and liquefaction steps. Research and development on an alternative enzymatic approach is thus of great potential for efficient utilization of cassava for ethanol.

Currently, an alternative non-thermal saccharification process has been developed at BIOTEC using the multi-enzyme composing of composite non-starch polysaccharide hydrolysing enzyme and raw starch degrading amylolytic activities produced from a selected fungal isolate in the BIOTEC Culture Collection. This allows direct saccharification of cassava pulp and also other cassava feedstock with no pre-gelatinization and liquefaction steps. The process leads to the efficient production of fermentable sugars, including glucose and xylose, with improving sugar yield and energy efficiency compared to the conventional acid or enzymatic processes. This multi-enzyme approach also results in viscosity reduction in the reaction medium. Together with the development of a high solid loading fermentation process and thermo-tolerant ethanol fermenting yeasts, the research will lead to the establishment of a cost-effective alternative bioprocess for production of biofuel and other value-added products from cassava.

Given the promising results to date from this research, a Thai patent application has been filed for the multi-enzyme and further research on multi-enzyme production and application in the bioreactor systems is currently in progress.



Saccharification of cassava pulp with multi-enzyme ENZ_Cas in comparison to commercial enzyme mixtures (ENZ1,2,3) (adapted from Rattanachomsri et al, 2009, J. Biosci. Bioeng.-in press)

THAILAND SCIENCE PARK

PROVIDING SUPPORT AND SERVICE

Set up in 2002, the TSP is a fully-integrated R&D hub for science and technology. It is managed by the Technology Management Center (TMC) of the National Science and Technology Development Agency (NSTDA) and is co-located with all of the NSTDA research centers, as well as being close to the Asian Institute of Technology and the Sirindhorn International Institute of Technology. This strategic location makes the TSP an ideal venue for research and development intensive companies looking to establish a base in Asia. Phase I of the Park is now fully occupied by NSTDA and more than 60 corporate tenants.

Phase II of the TSP is now well underway and will include features such as:

- Designated areas for laboratories requiring vibration control and special preparation.
- Specific areas at the base of the four new towers suitable for setting up equipment requiring floor loading allowance.
- Link-ways between the four towers to foster interaction and networking among the tenants.
- Direct access to the state-of-the-art Thailand Science Park Convention Center which includes 14 meeting rooms, an auditorium and a 2,000m^2 exhibition area.

Support Services

In addition to access to the resources of the NSTDA organization, tenants at the Park can also access the comprehensive range of support services available through TSP's Sales and Business Development team:

Technology & Technical Services

- Contract Research and Joint Research
- Testing and Analytical Service
- Technology Information Service
- Technology Licensing Service (In-licensing & Out-licensing)

Financial Services

- Application for Research Funding
- Application for Soft Loans
- Joint Investments

Human Resource Services

- Training and seminars on specific business and technology topics
- HR Recruitment
- Specialist database services

Business Support Services

- Intellectual Property Service
- Technology Licensing Office
- Business Matching Service
- Visa & Work Permit Assistance

For more information, please visit http://www.sciencepark.or.th.

Air Products Asia Food Technology Center

Air Products serves customers in industrial, energy, technology and healthcare markets worldwide with a unique portfolio of atmospheric gases, process and specialty gases, performance materials, and equipment and services. The company officially opened the Air Products Asia Food Technology Center at TSP in 2008. The Center has been established to provide innovative solutions and technical expertise to support the growing demands from the Asian food market. Air Products also aims to leverage expertise of Thai researchers in microbiology and food science.

The Alltech Asia-Pacific Biosciences Center officially commenced operations in the TSP in 2006.

The Center is committed to an active research program focused on the use of regionally important by-products for use in solid state fermentation and enzyme production. Understanding the important process of fiber digestion as it occurs in solid state fermentation is the cornerstone of the Center's research activities. Such research is designed to develop a range of natural enzyme complex that can be used to improve the digestibility of a variety of alternative raw materials. The Center also supports Alltech's expanding customer base in the region by providing technical laboratory support for research activities and analytical services when required.

MBS Asia
Immunobiological Services

In 2008, Maine Biotechnology Services, Inc, decided to open its first satellite facility at the TSP, to be called MBSAsia Ltd. MBS is a contract developer and manufacturer of monoclonal and polyclonal antibodies. Services provided include hybridoma development, polyclonal antibody development, ascites and in vitro production and purification. MBS also offers a large selection of bulk and OEM monoclonal and polyclonal antibodies for diagnostic, pharmaceutical and research applications.

The plan is for MBSAsia to be like its parent company and become a leading contract immunobiological service and antibody contract manufacturer. Services to be provided in their cGMP facility include hybridoma development, polyconal antibody development, ascites and *in vitro* production and antibody purification. MBS also plans to offer a large selection of bulk and OEM monoclonal and polyclonal antibodies for diagnostic, pharmaceutical and research applications.

Betagro Science Center

Betagro Group is one of Thailand's leading integrated agribusiness companies, developing and producing high quality products. Apart from focusing on modern production technology, the Group also places emphasis on research and development in a central laboratory - an important strategy in strengthening its competitiveness both in domestic and international markets. It also places a high degree of importance on the safety and quality of food products provided for customers.

With this in mind, the company established the Betagro Science Center in 2005 in the TSP. The Center aims to play a vital role as a centre of research and development with regards to animal feed, livestock and food products. Today, it is part of a collaborative network of private sector and academic institutes within the country and abroad.

The Center includes a Research and Development Center, divided into food, biotechnology, livestock, animal health products and others. There is also a Central Laboratory which supports the Group's core business and serves external customers in four main areas - pathological, bacteriological, virus & serology and chemical research and services. In addition, there are another two support functions - quality assurance and veterinary services.

Delphi Health Services, Ltd.

Delphi Health Services is a Thailand-based consulting and services firm specializing in biotechnology and medical care. Dephi's head office is in the US, while their research facilities are housed within the TSP.

Through their three main divisions, Delphi offers assistance to biotechnology companies seeking to establish a manufacturing, research or processing facility in Thailand. This includes providing a turn-key solution for US firms seeking to establish facilities in Thailand. Contract laboratory research is also provided for genotyping and plasmid services. Delphi Health Services specializes in human genotype testing technology and bioinformatics to detect predispositions to common diseases with complex genetic risk factors. The firm collaborates with research groups in Thailand and in the US to create computer models predicting relationships and interactions between common genetic variations and how these variations can be used to predict the onset of serious diseases. Currently, Delphi is testing assays against Type II Diabetes, Psoriasis and Eczema with an Alzheimer's project in development.

MAHIDOL UNIVERSITY

COMMERCIALIZATION OF INNOVATION

Mahidol University has its origins in the establishment of Siriraj Hospital in 1888 by His Majesty King Chulalongkorn and the hospital's medical school is the oldest institution of higher learning in Thailand, granting its first medical degree in 1893.

Mahidol University has since developed into one of the most prestigious universities in Thailand, internationally known and recognized for the high caliber of research and teaching by its faculty, and its outstanding achievements in teaching, research, international academic collaboration and professional services. This diversified institution now offers top quality programs in numerous social and cultural disciplines, including the most doctoral programs of any institution in Thailand, yet has maintained its traditional excellence in medicine and sciences. Much support has been given to stimulate research activities such as research funding, research facilities, international collaboration as well as graduate and post doctoral programs. Mahidol University is one of the top universities that produce the most number and most cited research publications in Thailand. As a leading research university, Mahidol is pursuing very active graduate and post doctoral programs.

With particular strength in the basic life sciences area, biotechnology research has been one of the top priorities at Mahidol. The university has invested heavily in providing modern research facilities and is active in pursuing international collaboration in research and teaching. All graduate and post doctoral programs are international.

Much of the research at Mahidol is focused on areas of particular relevance to Thailand, such as tropical disease prevention, tropical biodiversity, tropical plant, animal and microbial resources. The university provides sophisticated tools for research in areas such as molecular, genetic and protein engineering as well as nanotechnology. Mahidol also has a Center for Cassava Molecular Biotechnology, Centex Shrimp, an Institute of Molecular Biology and Genetics, the SEAMEO-TROPMED Center and an Institute of Nutrition. Most recently, a research team from the university was successful in developing a bacterial strain to produce a new generation pertussis vaccine.

Mahidol University provides commercial services related to life sciences and health. Three spin-off companies have been created to undertake business related to clinical trials of new drug developments. International Bio Service Co., Ltd is a unique, full service contract research organization for bioavailability and bioequivalence. International Drug Development Co., Ltd is a company that specializes in 1st and 2nd phase clinical field trial studies, whereas Aclires (Bangkok) Co., Ltd is a joint venture aimed at enhancing drug development through clinical trial phases I, II and proof of concept services. In the area of commercialization of innovation from research funding, Mahidol provides several key assistance activities such as entrepreneurship training programs, a business and technology incubator as well as a holding company (Stang Holding Co., Ltd.), that invests in new spin- offs arising from innovations created by researchers at the university.

For more information, please visit http://www.mahidol.ac.th.

CHULALONGKORN UNIVERSITY

A HIVE OF RESEARCH ACTIVITY

Chulalongkorn University is regarded as Thailand's premier institution and was founded over a century ago. As a national intellectual center, the university produces the finest quality graduates with a high level of knowledge and skills in the arts and sciences that they can use to contribute to society.

With the aim to be a pillar of the kingdom by creating of our own knowledge through multidisciplinary research on promising issues for sustainable development, Chulalongkorn University launches 5 research clusters; food and water, energy, climate change, emerging health risks and healthy aging society for sustainable development.

In terms of the sheer volume of research centers, institutes and units, the university would easily be Thailand's largest. Much of this research activity is devoted to biotechnology-related fields.

Institutes (from a total of 10): Institute of Health Research, Environmental Research Institute, Institute of Biotechnology and Genetic Engineering, Aquatic Resources Research Institute.

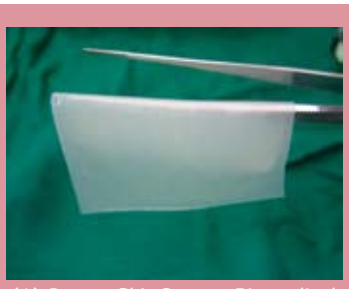
Centers of Excellence (from a total of 18): National Center of Excellence for Environmental and Hazardous Waste Management, Center of Excellence for Biodiversity Management, Center of Excellence in Viral Hepatitis, Center of Excellence for Marine Biotechnology, Center of Excellence in Entomology, Center of Excellence in Biodiversity.

Research Units (from a total of 100): Natural Product Research Unit, Computational Chemistry Research Unit, Research Center for Bioorganic Chemistry, Supramolecular Chemistry Research Unit, Organic Synthesis Research Unit, Amphibian and Reptile Research Unit, Primate Research Unit, Animal Systematics Research Unit, Starch and Cyclodextrin Research Unit, Shrimp Molecular Biology and Genomic Research Unit, Plants of Thailand Research Unit, Environment and Plants Physiology Research Unit, Clean and Green Fuel Research Unit, Bioremediation Research Unit, Sensor Research Unit, Genetic Engineering Research Unit, Enzyme Engineering Research Unit, Natural Rubber Research Unit, Food Safety and Quality Assurance research Unit, Environmental Assessment & Monitoring Research Unit, Bioactive Compound Research Unit, Biopolymer Technology Research Unit, Bio-Electronics Research Unit, Membrane Bioseparation Technology Research Unit, Leachate and Hazardous Waste Treatment Research Unit, Management of Industrial Waste Research Unit, Unit for Research and Development on Thai Abalone Aquaculture Technology, Chitosan Biomaterials Research Unit, Molecular Genetics for Medicine Research Unit, Biochemistry and Molecular Biology of Metabolic Disease Research Unit, Molecular Biology and Genetics of Cancer Development Research Unit, Research Center for Bioactive Marine Natural Products Chemistry, Pharmacological Action of Natural Products Research Unit, Natural Product Biotechnology Research Unit, Biomedical Analysis Research Unit.

Chulalongkorn is home of the first Halal Science Center in Thailand which provides analytical services for detection of any contamination's against Islamic law (Haram and Najis) in raw materials, and finished products supplied for halal food market, as well as conduct research and development on product innovation.

Chulalongkorn also has three other units supporting research; a Division of Research Development and Promotion, Unisearch, providing research services for both the government and private sector, and the Intellectual Property Institute, for managing all IP of the university.

For more information, please visit http://www.chula.ac.th.



(1) Pure Skin® - Biomedical engineering liked artificial skin

(2) 'Alnada'-Najis Cleansing Clay Liquid Detergent - Halal liquid detergent

(3) Bioceramics (porous calcium phosphates) - resorbable implant for hard tissue

KING MONGKUT'S UNIVERSITY OF TECHNOLOGY THONBURI

PIONEERS IN BIOTECHNOLOGY

KMUTT has an impressive research team that have developed a reputation for working closely with industry. Several successes have been noted in the fields of food technology, biogas, wastewater treatment technology, biosensors and, more recently, genomics and bioinformatics.

In developing a second campus in an industrial area on the outskirts of Bangkok, it was determined at an early stage that there should also be concurrent development of an industrial park. Work commenced in 1994 with a focus on small to medium scale enterprises that have excellent potential but lack the initial resources to compete and survive in the business world. Through the industrial park, such companies could have access to the human and material resources of the university, who in turn can provide the necessary support to help these ventures to grow and gather strength, with a target for independence within five years. In essence, the industrial park serves as an incubator for innovation.

The technology focus at the park includes food processing, biotechnology, energy and environmental technology, with expertise readily available for microbial bioprocessing, engineering properties of food materials, thermal and aseptic processing, cell culture and genetic modification/fermentation, *spirulina* mass cultivation and the production of biochemicals, waste utilization and management, bioprocess modeling and simulation, environmental biotechnology, energy conservation and clean energy technologies. The park helps fill the gap between research and its actual application in food and biotechnology industries, especially in microbial bioprocess development, by providing pilot scale applied research with various suites of fermentors in the range of 5 to 1500L. Conceptually, the park aims to fill the gap between demand pull (the technology needs from industry) and supply push (the innovation/ knowledge developed from research institutes). The conventional management system usually found in the universities does not currently facilitate such linkages.

Some of the successes to date have been:

- Pilot scale production of pressed yeast for Bioman Co. Ltd.
- Pilot scale production of *Bacillus subtilis* for probiotics market trials in the animal feed industry for Grand Siam Co. Ltd.
- Pilot plant fermentation services for microbial production applied to wastewater treatment in the shrimp farming industry for Grandness Integration Co. Ltd., Allvet Co. Ltd. and T.C. Union Co. Ltd.
- Cooperative research with Biowealth Co. Ltd. to conduct fungal fermentation for enzyme production to be applied for probiotics in the animal feed industry.
- Design, construction and operation of an industrial-scale anaerobic fixed bed reactor for wastewater treatment and biogas production for a rice starch factory [Bangkok Interfood Co. Ltd].
- Start-up anaerobic wastewater treatment plant and training for monitoring the system for a soft-drink manufacturer/bottler [Green Spot Company].

More recently the microbial production of biopharmaceuticals in Thailand was given a considerable boost following investment by the government in a cGMP Bioprocess Facility to be established at the park, designed to comply with USFDA standards.

The park is also host to numerous training activities organized on a continuing basis specifically for the private sector. These include such courses as; Animal Cell Culture and Applications, Mass Cultivation

of *Spirulina,* Bioinformatics as a Tool for Gene Manipulation, Metabolic Engineering and Functional Genomics, Fluorescence in situ hybridization for characterization of microbial cells without cultivation, Pilot scale utilization of wastewater from tapioca starch factory for tapioca starch factory entrepreneurs, Monitoring of Anaerobic Wastewater Treatment Systems for Agro-industries, Practical Approach to Fermentation Technology Workshop and a Regional Mini-symposium on Biosensor and Chemical Sensor Technology.

The campus also hosts the School of Bioresources and Technology, the Pilot Plant Development and Training Institute, the Excellent Center for Waste Utilization and Management and the Biochemical Engineering Pilot Plant Research and Development Unit. All of these facilities provide their support to the industrial park and are available to service the private sector. KMUTT is also active in hosting researchers and others from neighboring countries, providing training and allowing use of the facilities. Scholarships are also provided to these countries for full-time study.

For more information, please visit
http://www.kmutt.ac.th

BIOTEC
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Agricultural Biotechnology International Conference and Trade Exhibition Show

ABIC 2009

Agricultural Biotechnology for Better Living and a Clean Environment

22 – 25 September 2009
Queen Sirikit National Convention Center
Bangkok, Thailand

Scientific Conference Program:

Plant and Animal Biotechnology

The highlight topics are

- Achieving Large Scale Replacement of Petroleum by Cellulosic Biofuels without Impacting Food and Feed Production while Benefiting the Environment and Economies
  Prof. Stephen P. Long, University of Illinois, USA
- Manipulating Cell Separation Processes for Crop Improvement
  Prof. Jeremy Roberts, University of Nottingham, UK
- The Challenge of Enough Nutritious Food
  Dr. William James Peacock, CSIRO-Plant Industry, Australia
- GM Crop for Food, Feed and Energy
  Prof. German Spangenberg, Plant Biotechnology Centre, Australia
- Gene Technology for Grain Legume Improvement
  Dr. TJ Higgins, CSIRO Plant Industry, Australia
- Plant-Made Vaccines to Prevent Diarrheal Disease
  Prof. Charles J. Arntzen, The Biodesign Institute at Arizona State University, USA

Aquaculture Biotechnology

The highlight topics are

- Aquaculture: The Blue Biotechnology of the Future
  Prof. Patrick Sorgeloos, Ghent University, Belgium
- Genetic Improvement In Aquaculture Production
  Dr. John A.H. Benzie, Marine Biotechnology, Moana Technologies, USA
- Responsible Ecologically Sustainable Aquaculture in the 21st Century
  Dr. Albert G.J. Tacon, Hawaii Institute of Marine Biology (HIMB)/ Simon Fuge-Smith (FAO), USA
- Biotechnology for Environmentally Friendly Control of Shrimp Diseases
  Prof. Timothy William Flegel, Mahidol University, Thailand

Exhibition:

The Exhibition will showcase the latest development, products, and technology available. Exhibiting is a must for any company within the industry to increase awareness among the participants.

Keywords: Energetic participation guaranteed, contacts leading to collaborations, insights that accelerate direction of research

Registration:

www.abic.ca/abic2009

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