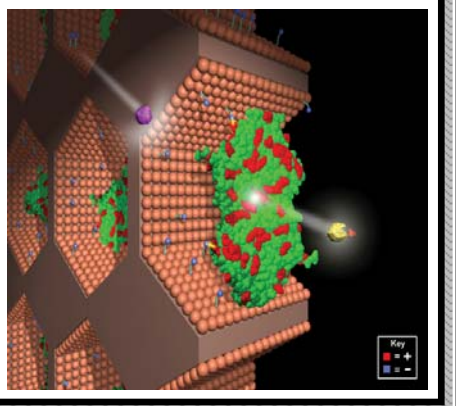

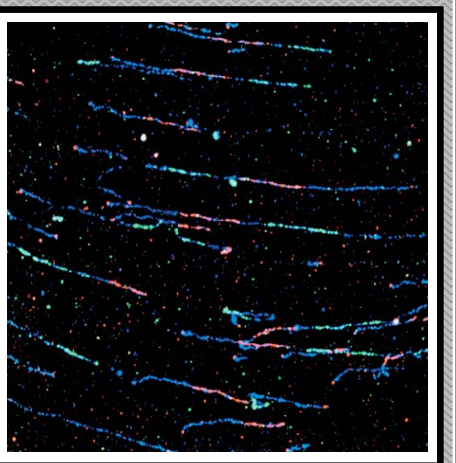

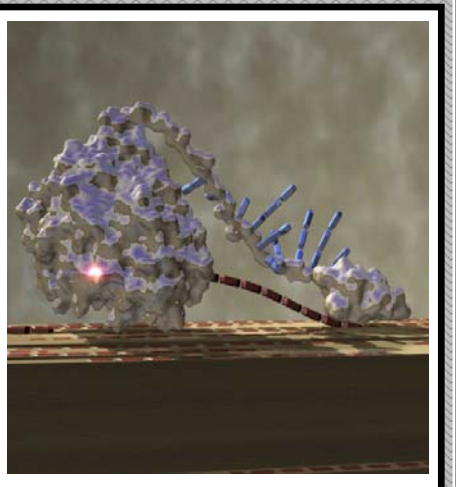

EMHGBN (EMGEN)* Newsletter

Vol. 2, Issue 9, September 20th, 2008

INSIDE THIS ISSUE:

Eastern Mediterranean Health Genomics and Biotechnology Network (EMHGBN) was created in 2004 with collaboration of representatives of selected centre of excellence in (health related) molecular biology, biotechnology & genomics in the Eastern Mediterranean region by recommendations and efforts of WHO/EMRO.

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* EMGEN is a shortened form of EMHGBN that was approved for the ease of use and future reference by the network steering committee.

Monoclonal Antibodies in Clinical Diagnosis

A Brief Review Application

An article entitled " Monoclonal antibodies in clinical diagnosis: A brief review application" aims to demonstrate the monoclonal antibodies for the diagnosis of viral disease, their application and current market in clinical sciences. The study was carried out by Muhammad Saleem Qazi and Mustafa Kamal. Corresponding author of this paper, Dr. Muhammad Saleem Qaz, is working in Pharmaceutical Research Centre, Pakistan Council of Sceintific & Industerial Research (PCSIR) Laboratories Complex, off. University Road, Karachi, Pakistan and the paper was published in African Journal of Biotechnology, 17 April 2008, Vol. 7 (8) pp 923-925.

The aim of present mini review articles is to demonstrate the monoclonal antibodies for the diagnosis of viral disease, their application and current market in clinical sciences.

Monoclonal antibodies have been an invaluable tool that has added to our biological knowledge for over a decade. Monoclonal antibodies (mAb) are important diagnostic reagents used in biomedical research, microbiological research in diagnosis of hepatitis, AIDs, influenza, herpes simplex, and *Chlamydia* infections and in the treatment of such diseases as infections and cancer.

The worldwide annual clinical diagnostics industry is valued at approximately $19 billion, with a growth rate of nearly 5% per year. In the worldwide market, the biggest areas of bulk sales are for immunoassays ($7.2 billion), clinical chemistry ($3.1 billion), hematology and blood gases (>$2.0 billion), and routine microbiology ($1.3 billion). Although a biochemical assay exists for almost every disease, diabetes is the largest single disease diagnostic category at $2.8 billion yearly (Hasulo, 2001). Historically, antibiotic and drugs in these therapy areas have driven biotechnology market evolution, and together they make up a significant proportion of total biotech market sales (Pijpers & Belsey, 2006: Churchill, et al., 2006).

Kohler and Milstein (1975) first developed the means for the production of monoclonal antibodies. After the first mAb production, a whole new era in the study of biotechnology was opened. Further this hybridoma technology has been improved over the years, particular by pre-selection of antigen-binding B cells and by screening with antigen-coating filters.

The modern popularity of the immunoassay is almost directly related to the development of recombinant mAb technology advancement. Hybridoma-derived or bacterially cloned monoclonal

antibody technology has enabled the mass production of highly specific probes for antigenic sites, whether on enzymes, receptors, hormones, or microbial products.

Antibodies have become common and essential research tools for many applications, including Western blotting, immunohistochemistry, immunocytochemistry, enzyme-linked immunosorbant assay (ELISA), immunoprecipitation and flow cytometric analysis. In addition, antibodies are now being designed for therapeutic applications, including suppression of the immune system after organ transplantation (Koch M. 2002 & Bumgardner, 2001) treatment of cancers such as leukemia, and inhibition of angiogenesis (Stephan, 2004).

More than 100 different monoclonal antibody diagnostic products are currently available (Janis, 1996). These larger varieties are used for routine diagnostic procedures and for therapeutic purposes. The use of mAbs in biomedical research has been and will continue to be important for the identification of proteins, carbohydrates, and nucleic acids. Their use has led to the elucidation of many molecules that control cell replication and differentiation, advancing our knowledge of the relationship between molecular structure and function. These advances in basic biologic sciences have improved our understanding of the host response to infectious-disease agents and toxins produced by these agents, to transplanted organs and tissues, to spontaneously transformed cells (tumors), and to endogenous antigens (National Research Council, 1999).

mAbs are important reagents used in biomedical research, microbiological research, in diagnosis of hepatitis, AIDs, influenza, herpes simplex, and in treatment of such diseases as infections and cancer (Hawkes, 2006). These antibodies are produced by cell lines or clones obtained from animals (*in vivo & in vitro*). *In vitro*, monoclonal antibodies form the basis of a number of diagnostic tests. For example, monoclonal antibodies against a hormone can detect pregnancy only 10 days after conception. Specific monoclonal antibodies are used for rapid diagnosis of hepatitis, influenza, herpes simplex, and *Chlamydia* infections.

Emerging technologies in novel antibody formats and mimetics will further provide opportunities to improve this unique class of biological drugs and will help to ensure their continued commercial success.

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Applying the Taguchi method for optimized fabrication of bovine serum albumin (BSA) nanoparticles as drug delivery vehicles

An article entitled " Applying the Taguchi method for optimized fabrication of bovine serum albumin (BSA)nanoparticles as drug delivery vehicles" aims to determine new optimized ways for farbrication of nanoparticles for drug delivery systems. The study was done by Mohsen Jahanshahi, Ghasem Najafpour and Mostafa Rahimnejad. Corresponding author of this paper, Dr. Mohsen Jahanshahi, is working in Nanobiotechnology Research Lab., School of Chemical Engineering, Babol University of Technology, Babol, I.R. Iran and the paper was published in African Journal of Biotechnology ,Vol. 7 (4), pp. 362–367, 19 February 2008.

Over the past few decades, there has been considerable interest in developing biodegradable nanoparticles (liposome, virus like particle (VLP), protein and etc.) as effective drug delivery devices.

Nanoparticles of biodegradable polymers can provide a way of sustained, controlled and targeted drug delivery to improve the therapeutic effects and reduce the side effects of the formulated drugs. Protein nanoparticles generally vary in size from 50-300 nm and they hold certain advantages such as greater stability during storage, stability *in vivo*, lower toxicity, non-antigenic and ease to scale up during manufacture over the other drug delivery systems.

In the recent work, coacervation method was used for manufacturing BSA nanoparticles as a colloidal drug delivery system and the essential parameters were considered by the Taguchi design method. In addition, the purification of nanoparticle products evaluated by SDS-PAGE and FTIR techniques while AFM and SEM characterized the shape and morphology of the products. This study was intended to establish a rational basis for the production and application of protein-based nanoparticles as drug carrier systems.

Therefore, BSA nanoparticles were fabricated successively exploiting robust process of coacervation. Physical and (bio)-chemical characterization of the nanoparticles were determined. According to the literature the results demonstrated that produced nanoparticles have sufficient properties as a carrier for drug delivery systems. A statistical experimental design method (Taguchi method with L16 orthogonal array robust design) was implemented to optimize experimental conditions of the purpose. Various factors affecting the particle size were analyzed and optimized where agitation speed and temperature have been shown to be highly influential upon the mean size of fabricated nanoparticle. By optimal conditions (at 500 rpm agitation, 4 °C temperature, pH 7.5 and 15 $mg.ml^{-1}$ BSA concentration) of this method, BSA nanoparticles (~74 nm) with narrow particle size distribution were prepared and these results were in good agreement with data analyzed by Taguchi method. Loading the drug on these nanoparticles will be the next step of the work and subject of further publication.

Factors	**Levels**			
A: Agitation speed (rpm)	200	400	500	600
B: BSA concentration (mg/ml)	5	15	20	30
C: pH	6	7	7.5	8
D: Temperature (ºC)	4	14	24	34

Table 1. Parameters and levels used in this experiment (Taguchi method).

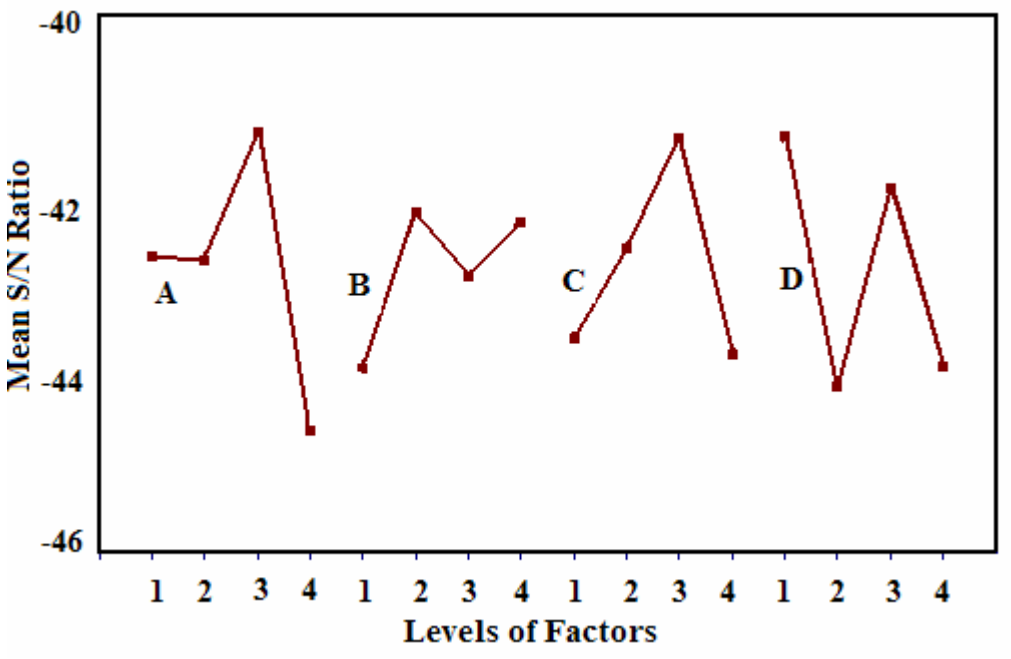

Figure 1. Response graph of S /N ratio for smaller-the-better analysis of nanoparticle size (Taguchi method).

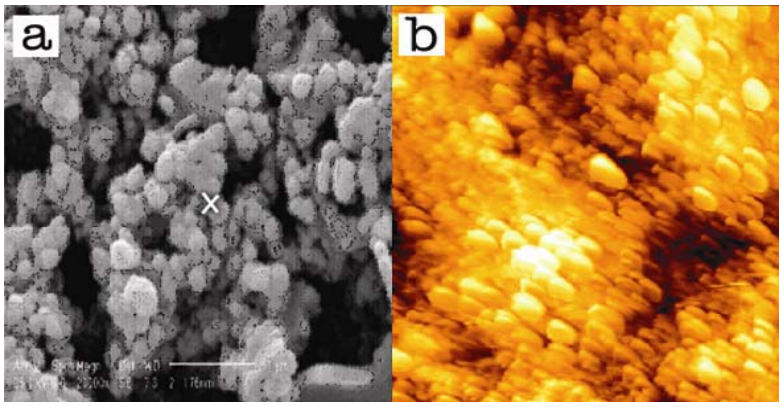

Figure 2. a) SEM image of BSA nanoparticle. The scale bars represent 1µm. b) AFM image of BSA nanoparticles. The smooth surface can be understood from the picture.

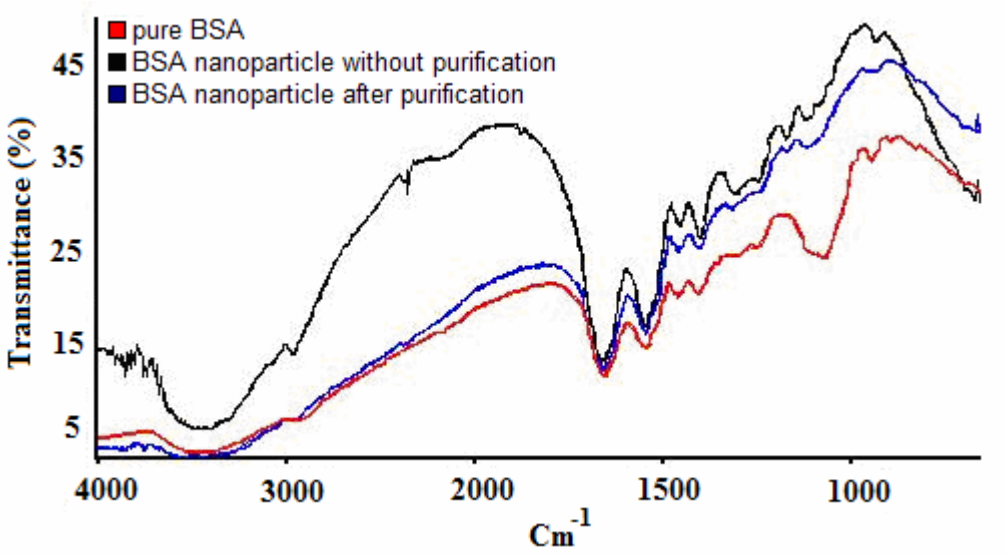

Figure. 3. FTIR analysis of BSA nanoparticle

Dear Researchers,

We are interested in reflecting on your research papers (from 2007 until present) or any reports about your work/research in laboratories, institutes or companies. We appreciate if you send us a brief description of your recent work in maximum 500 words and pictures. In addition, we require two pictures related to you and/or one or all of the contributors. Please send them in ".doc" or ".docx" format to one of the following email addresses:

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Metabonomics

Metabonomics is a new era of science concerning with the qualitative and quantitative understanding of the metabolites of a living system; how it respond to both endogenous and exogenous changes (such as physiology and xenobiotics, respectively). The goal here is to detect, quantify and list the metabolic processes of the whole biological system; what seems out of reach in a very near future. In other words, metabonomics trys to analyze metabolic pathways and responses in all life forms thoroughly. Different experiments in this field, including quantitative ones, are done with the help of complex analytical techniques such as NMR, GC-MS, LC-MS or FT-IR rate term metabonomics has a wide range of definitions made by different groups; but simply it can be summarized in the phrase: "solving the metabolome"; a complex space of interactions and components which we have just begun to explore.

Figure 1. 900MHz, 21.2 T NMR Magnet at HWB-NMR, Birmingham, UK being loaded with a sample.

Metabolites are intermediates and products of metabolism. Metabolites are mostly described as small molecules, with less than 2K Dalton molecular mass. Metabolic processes within a living organism are highly regulated by a variety of enzymes, which themselves are regulated by specific genes. Defect in each of the component mentioned, or interactions between them could cause chronic diseases in human, which can be very severe in some cases. Metabonomics is based on analysis of the normal and diseased state of metabolites and their pattern in individuals, which is a characteristic of them. It seems that this particular pattern can be applied for diagnosing diseases and predicting individuals' different responses to treatments. All drugs do not have same effects in all individuals and in rare cases "adverse drug reaction" can happen. As an example of how this can occur, a drug or its reactive metabolites might inhibit or inactivate enzymes regulating essential metabolic pathways, thus cause drug-induced toxicity. As metabolites are small molecules, they can specify a body's drug response. Considering this fact, metabonomics can be a great tool for identifying any abnormalities in normal state of metabolic processes. Using this approach as "advanced clinical chemistry" may provide more sensitive biomarkers for these abnormalities and also drug toxicity.

Sir Archibald Garrod was the first to research on metabolic disorders in the early 1900s, discovering various diseases including alkaptonoria, pentosuria, cystinuria, and albinism.To date more than 150 inborn genetic disorders have been characterized such as cystic fibrosis, hypothyroidism, sickle cell anemia, phenylketonoria and Tay-Sachs disease. Garrod published *Inborn Errors of Metabolism*, the first book on subject in 1908. After these early attempts, which were primarily ignored at that time, today metabonomics has been successfully applied to screen and treat newborn babies with errors of metabolism.

Here the latest advances of mass spectrometry and NMR should help move the safety evaluation of drug candidates into the new millennium. Potentially, this new technique is of huge importance to the future of healthcare and the pharmaceutical industry.

Metabonomics offer several advantages over genomics and proteomics:

1. It has a relatively small number of biomarkers (~2500-3000).
2. It can be applied non-invasively in biofluids (plasma, urine, feces, etc), which can be considered "expanded clinical chemistry".
3. Combined toxicogenomics and metabonomics data in animal models can help focus on evaluating metabonomics biomarkers of clinical relevance.
4. Several diseases, particularly those from inborn errors of metabolism, have been characterized with specific clinical biomarkers in relation to clinical path physiology.

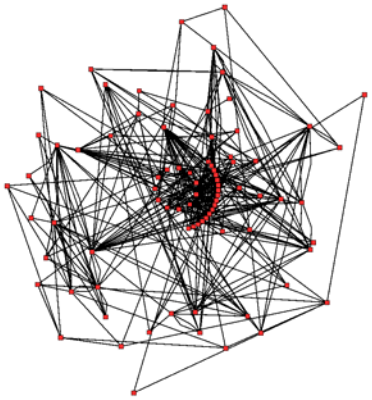

Figure 2. Metabolic network of the *Arabidopsis thaliana* citric acid cycle. Enzymes and metabolites are shown as red squares and the interactions between them as black lines.

The use of metabonomics as a tool has a rapid progress especially in pharmaceutical industry for discovery of new more efficient biomarkers. Using this approach for predicting responses to drug, is also an important new aspect of metabonomics applications and can contribute to understanding how patients might benefit from more individualized therapies, making the goal of personalized medicine more realistic. Metabonomics and specially its use as a clinical and diagnostic approach are in an early stage of development, but it has been thought that very soon it will bring about important progresses both in the healthcare and the science itself.

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Links for pictures:

1. http://en.wikipedia.org/wiki/Image:HWB-NMRv900.jpg
2. http://en.wikipedia.org/wiki/Image:A_thaliana_metabolic_network.png

Genetic Engineering and Biotechnology Research Institute (GEBRI)

In one of our former issues, we have introduced "Mubarak City for Scientific Research". In this issue we will discuss the departments and projects exist at GEBRI, one of research institutes in this city.
The institute is aiming to carryout biotechnology research to serve in different fields as: Medical, Environmental, Industrial and Pharmaceutical areas. This institute has established strong links with industry by implementing molecular techniques and incorporating biotechnological products and developing others for the sake of market benefits.

Departments of GEBRI:

Proteins Research Department (PRD)

PRD is specialized in executing researches related to proteins chemistry, protein structure and functions, protein engineering to modify its structure aiming to increase the efficiency of their performed functions, to produce components with high economical values. PRD teams try to catch the hi-tech technologies, like the protein crystallography, proteomics, NMR, modeling, and high-throughput screening machinery and using these technologies to find new economical-potential agents, to reshape or remove undesirable characters, to increase the activity or affinity, to miniaturize protocol and/or process. Currently PRD teams are working on recombinant antibody, protein biopolymers, lectins, and some important thermophilic enzymes.

Nucleic Acid Research

The department focuses on nucleic and research employing novel techniques for genomes studies, employing gene amplification, detection and transfer technology in different prokaryotic and eukaryotic systems, with the aim of optimization of the metabolic processes and traits of the organism. Research extends to biodiversity and germ plasm conservation, construction of genetic maps and Bioinformatics.

Medical Biotechnology

Medical biotechnology department is the department dealing with biomedical research in the field of diagnostic, prognostics, therapeutics, vaccines, and stem cell research.

Projects:

Formation of antibody display library against cobra neurotoxin

This project describes procedures to create a recombinant antibody (Fab) against short neurotoxin of cobra venom. The *in vitro* immunization is utilized to get the specific cDNA library-phage of the antibody for first time worldwide.

Polymorphism in immunogenetic factors involving disease symptoms in Egyptian HCV Infected Patients

Hepatitis C infection is one of the major health problems around the globe. This type of infection affects large number of Egyptians (~18-24%), and the Egyptian economy in an indirect way. The mechanism(s) that is responsible for viral clearance, response to treatment, and protection from its associated disabilities is unidetified yet. Several studies specified that variations in the immune response, including polymorphisms in the HLA and cytokines genes may have influence on the symptoms of HCV infection. Also, information about these genes involved in variations of the immune response of HCV infected patients with the detailed information about HCV genotype, subtypes and viral load will be of great help in the designing of an effective vaccine as well as identification of the type of therapy suitable for every individual patient. HLA class II (DRB1, DQA, &DQB) allele(s) or haplotype associated with chronic HCV infected patients, and chronic HCV infected patients with cirrhosis, in Egyptian population and examining the relationship between HLA class II gene polymorphism, viral load, genotype and disease symptoms are part of this project.

Development of microarrays for Evaluating Phylogenetic and Functional Diversity of the Microbial World

DNA microarrays technology is one of novel technologies in nucleic acids research. It permits the unique chance to study the genetic materials of living organisms with using a lot of DNA probes with quantitative and qualitative efficiency. It is well known that, there are many research techniques to study and detect the biodiversity and functional varieties of microorganisms but some techniques make limitation to survival ability of the microorganisms. Therefore, there is a critical need to use microarray technology to detect the biodiversity of microorganisms.

[ref link: http://www.mcsrta.sci.eg/InstitutePages/Home.aspx **]**

Genomic News from Jordan

In this issue, we have two news from Jordan, sent by Dr Sana' A. S. Al Hait - Head of department for prevention of genetic & congenital disorders, Ministry of Health - Jordan.

Community genetic programmes:

* Premarital Screening for thalassaemia became mandatory in June 2004. The programme has been updated; screening programme will include common Hb disorders in Jordan, thalassaemia and sickle cell anaemia.

It has been integrated in the free of charge health services. Prenatal diagnosis has not been affiliated to it, it has been requested voluntarily.

* New Born Screening for Hypothyroidism (HT) and Phenylketonuria (PKU) has covered all the country. It is a National Programme; a campaign for health educating the community and for raising awareness has started.

Both the test and the treatment of detected infants are free of charge.

Anouncement

4th Regional Conference on Medical Journals in the Eastern Mediterranean Region

5-7 November 2008, Manama, Bahrain

The 4th Regional Conference on Medical Journals in the Eastern Mediterranean Region will be held under the patronage of H.E. Dr Faisal Bin Yaqoub Al-Hamer, Minister of Health, Bahrain. The conference theme is:"Research and Publication are Cornerstones of Health Care Development in the Eastern Mediterranean Region"

You can register through "Registration" and fill out a form and send it online, or by email/fax. **Registration is free.** For more information you can visit the website.

The abstract submission will close on 31 August 2008. Registration closes on 20 October 2008.

Web address: http://www.emro.who.int/emame/emmj4/index.htm

Secretariat:

Tel: +973 17827818

Fax: +973 17827814

School IBSS'2008: International Bioinformatics Software

3 - 8 November 2008,Tangier, Morocco

The Moroccan association will organize the second international Bioinformatics software School IBSS'2008 from 3th to 8th November 2008 in Tangier, Morocco. IBSS'2008 will be the occasion to review and highlight the recent advances in Bioinformatics software, computing and algorithms. Topics:

- ✓ Systems biology
- ✓ Mathematical aspects of stoichiometric matrices
- ✓ Principles and analysis of protein-protein interactions and networks
- ✓ Data mining and statistical machine learning for molecular diagnostics
- ✓ Protein structure bioinformatics
- ✓ Creating, accessing and integrating bioinformatics databases
- ✓ Protein, Domain, Gene and Genome Families
- ✓ Databases, methods and applications
- ✓ Ontology

For more information you can visit the following web address:

Web Address: http://www.smbi-maroc.org/IBSS08/ibss08_1/

Cover Pictures Description (top to bottom)

Title: Synthetic Nanostructures: Putting Microbial Capabilities to Work.
Description: Understanding the sophisticated biochemistries of microbes can lead to the discovery of ways to isolate and use their components to carry out some of the functions of living cells. An example in this figure shows the enzyme organophosphorus hydrolase (OPH), which has been embedded in a synthetic nanomembrane (mesoporous silica) that enhances its activity and stability [*J. Am. Chem. Soc.* 124, 11242–43 (2002)]. The OPH transforms toxic substances (purple molecule at left of OPH) to harmless by-products (yellow and red molecules at right). Applications such as this could optimize the functionality of countless enzymes for efficient production of energy, removal or inactivation of contaminants, and sequestration of carbon to mitigate global climate change. The knowledge gained from GTL also could be highly useful in food processing, pharmaceuticals, separations, and the production of industrial chemicals
Source: http://genomics.energy.gov/gallery/gtl/detail.np/detail-49.html

Title: Nuclear Magnetic Resonance Spectrometer
Description: Environmental Molecular Sciences Laboratory's 800-MHz nuclear magnetic resonance spectrometer at Pacific Northwest National Laboratory.
Source: http://genomics.energy.gov/gallery/systems_biology/detail.np/detail-20.html

Title: FISH Mapping on DNA Fibers
Description: The fluorescence microscope reveals several individual cloned DNA fibers from yeast artificial chromosomes (YACs, in blue) after molecular combing to attach and stretch the DNA molecules across a glass microscope slide. Also shown are the locations of two P1 clones, labeled green and red, mapped onto the YAC fibers using FISH. Digital imaging technology can be used to assemble physical maps of chromosomes with a resolution of about 3 to 5 kilobases.
Source: http://genomics.energy.gov/gallery/basic_genomics/detail.np/detail-20.html

Title: Converting Cellulose to Sugars
Description: Cellulases include a mix of enzymes that break down cellulose into simple sugars that can be fermented by microorganisms to ethanol. Three general classes of cellulases-endoglucanases, exoglucanases, and cellobiases-work together in a coordinated fashion to hydrolyze cellulose. Endoglucanases internally cleave a cellulose chain, and exoglucanases bind the cleaved ends of the cellulose chain and feed the chain into its active site where it is broken down into double glucose molecules called cellobiose. Cellobiases split cellobiose to yield two glucose molecules. The cellulase pictured is an exoglucanase whose binding domain on the right extracts a cellulose chain. At the active site in the larger catalytic domain on the left, the cellulose chain is hydrolyzed to yield cellobiose subunits. [Image from M. Himmel et al., “Cellulase Animation,” run time 11 min., National Renewable Energy Laboratory (2000).]
Source: http://genomics.energy.gov/gallery/gtl/detail.np/detail-47.html