

### EMHGBN Newsletter Vol. 2, Issue 6, May 25<sup>th</sup>, 2008

### **INSIDE THIS ISSUE:**

- 1. Articles, P2
- 2. Trends, P5
- 3. Training, P9
- 4. Biotech centre, P13
- 5. Announcements, P16
- 6. Cover pictures description, P17

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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# **Articles**

### Natural Bioremediation of Heavy Metals through Nematode Parasite of Fish

The article entitled "Natural Bioremediation of Heavy Metal through Nematode Parasite of Fish" aims to indicate the bioaccumulation potential of heavy toxic metals by atomic absorption Spectrophotometry which was assessed in the Echinocephalus sp. and Ascaris sp. and reported as natural bioremediator of heavy metals in Karachi coast. The high level of toxic metals in Echinocephalus sp. and Ascaris sp. and Ascar

these nematode parasites are sensitive indicator of heavy metals in aquatic ecosystems. The study was done by Dr. Rafia Azmat, Shahina Fayyaz, Nasira Kazi, Syed Junaid Mahmood, and Fahim Uddin. Corresponding author of this paper, Dr. Rafia Azmat is working in Jinnah University for Women Department of Chemistry Karachi, Pakistan and The paper was published in Biotechnology 7 (1): 139-143, 2008. This journal is accessible through Asian Network for Scientific Information.



Dr. Rafia Azmat (back) and Dr. Shahina Fayyaz (front)

Parasites are naturally occurring organism, attracting increasing interest as a potential indicator of environmental quality and remediator of environmental pollution in variety of ways by which they respond to anthropogenic pollution. As a matter of fact, the deteriorating state of the environment in aquatic resources is reflected by increased degree of parasites. Similarly with these views, present studies have been launched in which nematode parasites were selected from fish parasites community for the reason that fish is an intermediate host of these parasites. Recovered nematodes from guts of infected fish were identified as *Echinocephalus* spp. and *Ascaris* spp., which were found to be common parasites of fish (*Liza vaigiensis*) of Karahci coast. The identification and photography of fish nematodes were made with the assistance of Dr. Rafia Rehana, Dr. Shahina Fayyaz and Dr. Nasira Kazi, National Nematological Research Centre, University of Karachi. Heavy metals analysis of water (collected from fishing zone), muscles, guts of infected and non infected fish and parasites was performed by using Atomic Absorption spectrophotometry. Highest heavy metal accumulation was reported in nematodes whereas infected fish showed a reduced amount of trace metals as compared to non infected one.

This leads to imply that community of nematodes is remediating the heavy metals (pollutant which is in priority because of its persistence) by accumulating these in their soft body tissues inside the body of fish, thus providing the support in survival of fish in heavy metal polluted water reservoirs. Specifically the concentration of Pb in both parasites showed that level of Pb is appreciably high in comparison with fish muscles and guts.





# Articles

The high level of toxic metals in both parasites (*Echinocephalus* spp. and *Ascaris* spp.) within its host recommended that these parasites are sensitive indicators of heavy metals in aquatic ecosystem, sharing more burden of environmental pollution of marine resources in their bodies and also acting as a natural bioremediator of toxic metals in fish. The parasitic infection rate in fish is often considered as an indicator of the degree of immunity of an organism. Recent investigations were supported by the results of earlier researchers, who reported more heavy metal burden like Pb, Cd, Cr, and Ni in parasite – host system in cyprinid fish. Similarly intestinal *Acanthocephalus* of fish reported as having capability to accumulate significantly high amount of metal in their soft bodies as compared to host muscles. Therefore, it may be concluded that parasites can minimize site disturbance within fish body as compared with conventional cleanup methods.



Recovered nematodes as a bio-remediator

### Efficient Downregulation of *alb1* Gene Using an AMA1-Based Episomal Expression of RNAi Construct in *Aspergillus fumigatus*

The article entitled " Efficient Downregulation of alb1 Gene Using an AMA1-Based Episomal Expression of RNAi Construct in Aspergillus fumigatus" aims to indicate the hairpin structure in episomal RNAi silencing cause downregulation of alb1 gene in Aspergillus fumigatus. The study was done by Vahid Khalaj, Hamid Eslami, Mohammad Azizi, Nuria Rovira-Graells, and Mike Bromley. Corresponding author of this paper, Dr. Vahid Khalaj is working in Biotechnology Research Centre, Pasteur Institute of Iran, Tehran, Iran and the paper was published in FEMS Microbiology Letters Volume 270 Issue 2 Page 250-254, May 2007.



# Articles

An episomal RNAi silencing construct containing the inducible cbhB promoter and a hairpin structure has been made to downregulate the *alb1* gene in the human pathogen *Aspergillus fumigatus*. Transformation of fungal protoplasts resulted in a high number of transformants with an inducible silenced phenotype (white spores). Efficient downregulation of the *alb1* gene using this system suggests that this approach may overcome the variable downregulation observed with integrative constructs.

The presence of RNA silencing machinery in filamentous fungi (Nakayashiki, 2005), including

A. fumigatus, has led to the successful application of RNAi methodology to downregulate both essential and nonessential genes in these organisms. However, these studies reported various degrees of interference by integrative construct that could be the result of random integration of the construct in different positions in the genome or due to rearrangement of the construct and loss of the transcriptional unit of RNAi during integration. In *Aspergillus* species, autonomous maintenance in *Aspergillus* (AMA1)-based plasmids have been successfully used in episomal expression of different constructs (Aleksenko and Clutterbuck, 1995, 1997; Aleksenko *et al.*, 1996).

The high frequency of transformation and relatively high copy number of plasmids in the nuclei suggest that an AMA1-based plasmid system may overcome many of the problems experienced with integrative plasmids. The efficiency of an AMA1-based episomal RNAi construct in downregulation of the *alb1* gene which involves in spore pigmentation in *A. fumigates* was examined (Tsai *et al.*, 1998, 1999). A silencing construct containing an inverted repeat fragment of the *alb1* gene separated by a 100 bp GFP buffer was prepared. To control the expression of this hairpin fragment, the cbhB promoter of *A. fumigatus*, which drives high levels of expression in carboxymethylcellulose medium and is not expressed in glucose medium (Bromley *et al.*, 2006), was used.

This cassette was introduced into the pRG3-AMA1 plasmid to make replicative plasmid pAMA-Alb1. To provide a comparator, the same cassette was placed in an integrative plasmid pALBR2. An AF293 *pyrG* strain was transformed with pAMA1-Alb1. This transformation was much more efficient, in comparison with integrative construct, resulting in several hundred transformants from a single reaction. These transformants exhibited green spores on noninducing media but unlike the result with the integrative plasmid, all isolates had white spores on inducing media, indicating complete repression of the *alb1* gene. RT-PCR analysis was performed on an RNA sample from one of these isolates grown on carboxymethylcellulose for 40h. No PCR product was identified, confirming silencing of the gene.



Dr. Vahid Khalaj





#### **Systems Biology: the Science of Future**

Systems biology is the study of an organism, viewed as an integrated and interacting network of genes, proteins and biochemical reactions which give rise to life. Instead of analyzing individual components or features of the organism, such as sugar metabolism or a cell nucleus, systems biologists concentrate on all the components and the interactions among them, all as part of one system. Systems biology emerged as the result of the genetics "catalog" provided by the Human Genome project, and a growing understanding of how genes and their resulting proteins give rise to biological form and function. The study of systems biology has been aided by the ease with which the internet permits researchers to store and distribute huge amounts of information, plus advances in powerful new research technologies, and the infusion of scientists from other disciplines, e.g. computer scientists, mathematicians, physicists, and engineers. Traditional biology — the kind most of us studied in high school and college — has focused on identifying individual genes, proteins and cells, and studying their specific functions. But that kind of biology can yield relatively limited insights about the human body.

As an analogy, if you wanted to study an automobile, and focused on identifying the engine, seat belts, and tail lights, and studied their specific functions, you would have no real understanding of how an automobile operates. More importantly, you would have no understanding of how to service the vehicle efficiently when something malfunctions. Biologists, geneticists, and doctors have had limited success in curing complex diseases such as cancer, HIV, and diabetes because traditional biology generally looks at only a few aspects of an organism at a time. As scientists have developed the tools and technologies which allow them to delve deeper into the foundations of biological activity — genes and proteins — they have learned that these components almost never work alone. They interact with each other and with other molecules in highly structured but incredibly complex ways, similar to the complex interactions among the countless computers on the Internet. Systems biology seeks to understand these complex interactions, as these are the keys to understanding life. Understanding the interaction of an organism's genome and environmental influences from outside the organism (nature and nurture) is crucial to developing a — systems understanding of an organism that will ultimately transform our understanding of human health and disease. Systems biology is still in its infancy; we are at the turning point in our understanding of what the future holds for biology and human medicine.

#### Systems definition and some of its attributes

A system is a group of parts that come together, interacting and interdependent, to form a more complex whole unit. In summary, systems are comprised of parts which interact. The interaction of these parts gives rise to new properties and functions which are keys to the system. We call these new properties and functions "emergent properties". Because emergent properties are the result of interactions between the parts, they can not be attributed to any single parts of the system.



# Trends

This makes systems irreducible. A system is unlikely to be fully understood by taking it apart and studying each part on its own. (We cannot understand an author's message by studying individual words; we cannot appreciate a forest by looking at individual trees.) To understand systems, and to be able to fully understand a system's emergent properties, systems need to be studied as a whole.

#### Using model organisms

Let us consider what happens to the number of possible interactions as the number of parts of a system increases. In the simplest case, a system has just two parts, and there can be only one interaction between these two parts. However, among a class of 20 students there can be 190 possible interactions, counting just the pair wise interactions. And among the approximately 25,000 genes that comprise each human being, there are more than 336 million possible pair wise interactions... since genes interact in more than pairs, the total number of possible interactions is staggering! Obviously, some simplification is essential for us to approach understanding a system of such potential complexity. We are mindful of the total number of possible interactions among the parts in an organism. There can be thousands, even tens of thousands of genes and proteins interacting within an organism to trigger some function in an organism. Fortunately, for research scientists, biological processes have been found to work exactly the same in many different organisms. So scientists can use simpler organisms for their initial studies of biological systems. We call this sort of simpler study case a "model organism". Studies on model organisms are crucial to eventually answering the central biological questions regarding human life. Because the complexity of biological systems is too immense to be understood by only a single discipline of science, we should rely on the expertise of scientists from multiple disciplines to probe and fully understand the properties of biological systems.

#### Introduction to disease

In "systems" terms, disease represents a disruption of one or more parts of a biological system, which in turn disrupts the interactions among various parts of the system, and thus compromises one or more of the system's functions (i.e., one or more of the system's emergent properties). Developing an understanding of the factors that cause disease motivates much of biological research. Historically, biologists studied organisms "from the bottom up". Because the complexity of biological systems can be overwhelming (even when studying a single human cell), scientists elected to dissemble the systems and study them, part by part, with the hope that the sum of their knowledge about the parts would help to elucidate the operation of the whole. Rarely has that been a successful strategy to understand the causes and cures for complex diseases, such as cancer. All biological organisms exhibit systems properties. Because of the potential complexity of a whole system, to truly understand biological organisms they must be studied as whole systems. We also must view the parts of an organism (including humans) as elements interacting in a unified system to fully understand that organism. This is the inspiration and driving motivation for systems biology discipline.



# Trends

#### Health Care in the 21<sup>st</sup> Century: Predictive, Preventive and Personalized

The objective of systems biology is to fundamentally transform the practice of medicine. Scientists are developing tools and techniques, and pursuing research that will usher in a new era of predictive, preventive, and personalized medicine. Today's medicine is reactive. We wait until someone is sick before administering treatment. Medicine of the future will be predictive and preventive, examining the unique biology of an individual to assess their probability of developing various diseases and then designing suitable treatments, even before the onset of a disease. Today's medicine is also myopic: we use only a few measurements to diagnose disease and are generally unable to make fine distinctions between individuals or between subtle variations of the same disease. Medicine of the future will use more sophisticated measurements, as well as more measurements overall, thereby yielding accurate health assessments for truly personalized treatments. In case of disease, we know certain defective genes will increase the probability of an individual having certain health problems. For example, a woman with a single copy of the mutant breast cancer 1 gene (BRCA-1) has a 70 percent chance of developing breast cancer by the time she is 60 years old. Unfortunately, today there is no practical way for each of us to recognize our genetic makeup and, more important, to understand the likely health consequences. However, in the future individuals will be able to easily obtain such information, and then work closely with their health practitioner to develop a predictive, preventive and personalized health-care program.

#### Prediction

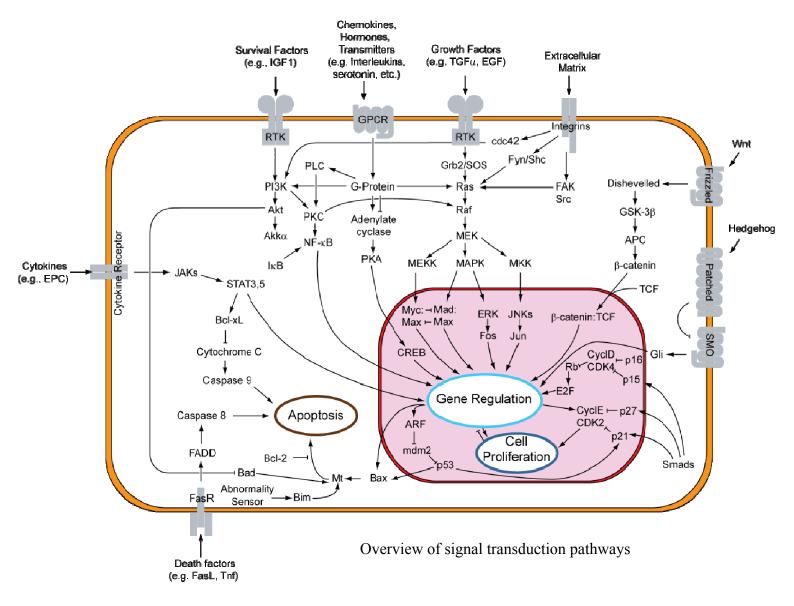
The technologies and tools of systems biology will provide medical practitioners with two exciting sources of health-related diagnostic data: by examining an individual's complete genetic makeup, a physician will be able to generate comprehensive predictions about the patient's health prospects. By examining biomarkers which naturally occur in an individual's blood, a physician will be able to precisely determine a person's health status, including both the current effects of any abnormal genes and the current reactions to any environmental toxins or infectious pathogens.

#### Prevention

The new approach to medicine, based on each individual's genetic makeup, will help us determine the probability of an individual contracting certain diseases, as well as reveal how an individual may respond to various treatments, thereby providing guidance for developing customized therapeutic drugs. Thus another application of the technologies and tools of systems biology will be to develop preventive treatments for individuals, based on their potential health problems, as indicated by their genetic makeup and current blood- protein markers.



The goal of this new approach to medicine will be to use the most fundamental health-related information — an individual's genetic makeup plus current health status (as identified by blood protein markers) — to prescribe appropriate preventive drugs. For example, given your genetic makeup, you may have a 40% chance of developing breast cancer by age 50, but if you start taking a certain drug at age 35, that chance could drop to 5% at age 50. In the next issue of our newsletter we will give you a more in depth view of systems biology and we will discuss some topics such as methodologies, promises, challenges and perspectives of systems biology.



[Ref: http://www.systemsbiology.org/Intro\_to\_ISB\_and\_Systems\_Biology]



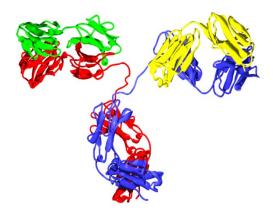


### Antibody engineering for clinical applications

Molecular engineering has contributed immensely to the clinical success of antibodies in recent years. The modular structure of antibodies has allowed their modification in several ways, to meet various clinical requirements. With the help of antibody engineering, it has been possible to modify the molecular size, pharmacokinetics, immunogenicity, binding affinity, specificity and effector function of antibodies. Moreover, fusion proteins of antibodies with various proteins and peptides have yielded targeted biological modifiers, toxins and imaging agents. Here we focus on the recent trends in antibody engineering for improving their clinical utility.

#### Introduction

Almost a century ago, antibodies were envisioned as 'magic bullets' for the specific targeting of a disease site. The recent success of antibodies in clinics has justified this reputation and has revolutionized treatment choices for various diseases. Antibodies can be used as unarmed therapeutic agents that inhibit a target involved in disease progression or by causing the cytotoxic death of target cells, mediated by modulators of the immune response. Alternatively, antibodies can act as carriers to target cytocidal and



imaging agents, such as radioisotopes, toxins, and drugs, to the site of a disease. The diverse clinical applications of antibodies have necessitated their modification in a variety of ways, thus laying the foundation of antibody engineering. Out of \_20 antibody-based products approved by the Food and Drug Administration (FDA) for human use, 85% are the fruits of antibody engineering. In this article, we have highlighted the recent developments in the field of antibody engineering that have helped in the clinical advancement of these magic bullets.

#### Antibody engineering for desired pharmacokinetics

The pharmacokinetic requirements of a given antibody depend upon the nature of its application. In the case of therapeutic antibodies, which generally act either by inhibiting a signalling pathway or By inducing antibody-dependent cell-mediated cytotoxicity (ADCC) or complement-dependent cytotoxicity (CDC), a prolonged serum half-life is desirable, for longer bioavailability and to avoid repeated injections (making it cost effective). Alternatively, if an antibody is being used as a vehicle for the delivery of a cytotoxic agent, such as a radionuclide, drug or toxin, the rapid elimination of the untargeted conjugate is preferable, to avoid nontarget-tissue toxicity.



## Training

In general, intact antibodies and antibody fragments >60 kDa are above the renal threshold and exhibit prolonged circulation, whereas smaller antibody fragments (<60 kDa) exhibit a shorter serum half life.

#### Small antibody fragments – from IgGs to scFvs

Antibody engineering started with the development of antibody fragments encoded by a single gene, wherein only the regions involved in antigen binding – the variable heavy (VH) and light (VL) chains – were linked by a short peptide. The resulting protein was called a single-chain Fv (scFv) and was monovalent in binding. In general, the affinity of a given scFv is comparable with the parental Fab fragment but owing to their monovalent binding such antibodies are of limited therapeutic significance. However, because of their small size (30 kDa), most scFvs have a short serum half life (<10 min) compared with the intact IgG, which can make them useful for diagnostic applications such as imaging. Nanobodies, which are derived from the VHH domains of heavy-chain antibodies, are the smallest antigen-binding domains and have recently generated enthusiasm. Nanobodies have been recently generated against various tumor antigens, including MUC1 and EGFRvIII, and exhibited tumor targeting in animal models. Multimerization of antibody fragments was undertaken to improve their serum half-life and also binding affinity and/or avidity. The initial strategies for multimerization relied on the use of linkers or the spontaneous formation of dimmers or higher-order structures. Other approaches also exist that we do not mention here.

#### Antibody engineering for reducing immunogenicity

Mouse monoclonal antibodies, when administered in humans, elicit a human anti-mouse antibody (HAMA) response that can alter their biodistribution and accelerate clearance, thus reducing the efficacy of subsequent administrations. To reduce their immunogenicity, antibodies are engineered in several ways. Here we only describe the latest technological advancements in this area. One approach is the use of transgenic mice, in which the mouse immunoglobulin loci are inactivated and replaced with human immunoglobulin genes. Several groups have developed various mouse strains using different transgenic methodologies. One such group is Xenomouse (Abgenix; http://www.abgenix.com). Panitumumab, directed against EGFR and generated using Xenomouse, was recently approved for the treatment of metastatic colorectal cancer. Advances in phage display technology have provided another route for the development of fully human antibodies. Adalimumab, an anti-TNFa antibody, was developed using a human phage-display library and has been approved for treating rheumatoid arthritis. Approximately, 15 fully human antibodies derived from phage libraries and directed against as many antigens are in clinical trials for the treatment of asthma, autoimmune diseases and various malignancies.



## Training

#### **Bispecific antibodies**

Naturally occurring antibodies are directed against a single antigen: they are monospecific. Advances in antibody engineering and expression methodologies have made it possible to combine the specificities of two antibodies into a single molecule, called a bispecific antibody (BsAb), for various clinical applications. There are several ways in which antibodies specific for two or more antigens can be generated. Here, we just highlight one of the recent approaches for the generation of BsAbs. Rossi et al. described an elegant approach, called the 'dock and lock' method, to generate a trivalent BsAb and demonstrated its utility in a pretargeting approach. Using the dimerization and docking domain (DDD) of the R subunit of cAMP-dependent protein kinase (PKA) and the anchoring domain (AD) of the Akinase anchor proteins, a stable, bivalent, anti-CEA-monovalent anti-HSG was generated for pretargeted radioimmunotherapy. The main advantage of this system is that an antibody fragment of any specificity can be produced, separately, as fusion proteins with either DDD or AD and, when needed, a simple mixing of the two purified products will give the desired BsAb. Ertumaxomab is an intact trifunctional, BsAb which has recently entered phase I clinical trial for metastatic breast cancer.

#### Antibody fusion proteins for biological activity

Fusion constructs comprising antibodies and proteins or peptides have been generated for various therapeutic applications. Abbreviations: CLL- chronic lymphocytic leukaemia; GM-CSF-granulocyte macrophage colony stimulating factor; NHL- non Hodgkin's lymphoma; PE- truncated Pseudomonas exotoxin A; TAT- transactivator of transcription. Antibody molecules in the fusion constructs are generally used to direct therapeutic agents, such as toxins, cytokines or a drugactivating enzyme, to the tumor microenvironment. Here we give an example of an immunoconjugate which is consisting of a fusion protein and antibody.

Owing to their immunomodulatory and anti-tumor effects, various cytokines (e.g. IL-2, TNFa, IFNg and GM-CSF) have been explored as therapeutic agents, either alone or in adjuvant settings. Unfortunately, their clinical application has been hampered owing to their high degree of systemic toxicity, when administered in physiologically relevant doses, their relatively short serum half-lives and their inability to target tumors specifically. Antibody–cytokine fusion proteins were developed to circumvent these hurdles and to deliver the cytokines specifically to the disease site, with a relatively prolonged half-life and reduced systemic toxicity. Antibody–IL-2 fusion proteins are in phase I clinical trials for the treatment of melanoma and neuroblastoma, and in preclinical studies for improving RIT. Several peptides have also been fused to antibodies for various applications. Fusion proteins of scFvs with a cell penetrating peptide have been used to inhibit intracellular targets.





### Training

An anti-Bcl-2 scFv tethered to a cell-penetrating peptide TAT was shown to neutralize the activity of Bcl-2 in mast cells and induce apoptosis. Also another interesting application of antibody engineering is in targeting antisense, siRNA and genes.

For the antibody engineer, there may be a special opportunity to revitalize the field of antisense technology as well as other oligonucleotide agents, such as siRNA and micro RNA (Ikeda and Taira, 2006). In one study (Song et al., 2005), Fab or scFv fusion proteins with a protamine domain were engineered to deliver target-specific siRNA to HIV infected cells or HER2 expressing cells in cell culture and animal models. Major breakthroughs in oligonucleotide delivery are anticipated in the coming decade and antibody engineering may be at the centre of this undertaking.

#### **Conclusion and perspectives**

The engineering of antibodies has contributed enormously towards their clinical advancement. The Pharmacokinetics of antibodies could be prolonged or shortened, which in case of shortening, this goal could be achieved by the generation of small antibody fragments. The immunogenicity in humans has been reduced by several methods and fully human antibodies, developed using transgenic animals and human antibody libraries, have been approved for clinical use. Several novel approaches have been recently described for the generation of BsAbs. The advances in display technologies have facilitated the rapid screening of antibodies in Fab, scFv or single-domain formats.

The generation of fusion constructs of antibodies with various proteins (e.g. biological modifiers and toxins) and peptides have further diversified the clinical application of antibodies. Of the 266 approved drug targets from the human genome, only 15 targets are approved for therapeutic antibodies for various diseases, and almost all of the targets of these antibody-based therapeutics are cell surface antigens. With the advances in the approaches to discover antibody frameworks that are stable and function intracellularly, and also the capabilities to transduce antibodies. Such advancements are expected to increase the number of possible antibody targets. Antibodies are, undeniably, set to have a more dominant role in disease management in years to come.

[**Refs:** 1) Maneesh Jain, Neel Kamal and Surinder K. Batra, Engineering antibodies for clinical applications, Trends in Biotechnology Volume 25, Issue 7, July 2007, Pages 307-316

2) David Filpula, Antibody engineering and modification technologies, Biomolecular Engineering Volume 24, Issue 2, June 2007, Pages 201-215]



# **Biotech center**

### The National Centre of Biotechnology (Jordan)

The National Center for Biotechnology is a virtual center with the recent developments in communication, it became theoretically feasible to stimulate collaboration in Science and Technology without having to set people in the similar building but providing them with connections and finances. This is what is now identified as a virtual institute. The most important vision is to try to catalyze this improvement in the field of biotechnology. The Board of the Higher Council of Science and Technology (HCST/Jordan) in its conference on 2/12/2003 accepted the establishment of a Virtual Institute of Biotechnology and delegated to the Secretariat General of the council the establishment of this institute. The committee of ministers approved by-law and a Royal decree was issued on November 1st 2005 (official Gazette No. 4726)

#### How this Centre Operates

• Making a database identifying particular capabilities of scientists in biotechnology.

Putting this on this website so that scientists can cooperate directly.

• Holding brain storming meetings with scientists in similar or complimentary fields to identify achievable economically-viable projects, and forming sub-committees to look into each of them.

(That is why at the present time we are limiting our activities to Jordan and near Arab countries).

• Each of the sub-committees presents its conclusions to the whole group where they are discussed and refined. (Scientists are paid a nominal fee for every session they attend).

• Possibly providing a small fund to test an idea, or for a patent when possible.

• Helping to produce a pre-feasibility study for the most promising plans.

• If the pre-feasibility is promising, getting a professional to produce a detailed feasibility.

If all goes well, looking into outlining a company with the involved scientists, institutions, and the private parts as partners.

#### Mission

The virtual institute does the following:

• Create and develop a knowledge map in biotechnology.

• Establish a searchable web site database for expertise, and make these accessible to all members.

• Manage meetings of people in a specific field to brainstorm, develop ideas, and stimulate cooperative research.







# **Biotech center**

- Help economic cooperative research and short exchange meetings.
- Help in developing a feasibility study for a project and a business plan.
- Help in obtaining financing to begin an identified feasible project.
- Help in obtaining patents.

• Help in strengthening the ties between academic institutions and commercial companies in the country.

#### Grants

#### Instructions

The National centre of Biotechnology has limited funds and will only finance projects in technology (and not pure science). Projects which are designed, lead to technological applications in a short time are given priority and so are projects with budget from other donors and/or applying for funds to finance projects to be undertaken jointly between more than one institution.



#### Cooperation

#### **Regional Cooperation**

The Centre represents Jordan in The Arab centres for Biotechnology. The Center established a Commercially Viable Company (MonoJo).

#### **International Cooperation**

In 2005 NCB submitted five research proposals to the European Union for financial support. The submitted proposals were in different fields of biotechnology. Commercial products are expected as yields of such projects.

• Production of Camel Heavy Chain Antibodies (Nanobodies) for Diagnostic Purposes of Human Cancers.

- Production of therapeutic monoclonal antibodies against chronic Candida albicans infections.
- Production of Novel Monoclonal Antibodies against Endemic Plant Viruses.

• Sequence analysis of the common local avian influenza (H9N2) isolates for possible use in monoclonal antibody or DNA vaccine production.

Negotiations are underway with UNDP, ESCWA, Helsinki University and US Trade Department.



# **Biotech center**

#### **MONOJO** in Words

1. MONOJO is a private sector profit-oriented, excellence-driven business firm specialized in the development, production and marketing of cell lines and antibodies.

2. It was formally established in Feb 2005 with an investment capital of JD 400000 at the Jordan Ministry of Industry & Trade.

3. MONOJO is a partnership between the Jordan Higher Council for Science and Technology, The National Biotechnology Centre, the Jordan Royal Scientific Society, Jordan University of Science and Technology, Philadelphia Private University, private investors and academic scientists.

4. We have rented a 500 square meter spaces in a building close to the Royal Scientific Society, in which the company and its state of the art laboratories will be housed.

#### What do MONOJO do?

1. Production and marketing of polyclonal as well as monoclonal antibodies for an extensive range of clinical and research applications. The firm will start with the production of a number of monoclonal antibodies that will come as in bulk, purified unlabeled or purified labelled. Antibodies to be produced are for diagnostic purpose, typing and diagnosis of diverse forms of cancer will be receiving particular emphasis.



2. Development and investment in new hybridomas and cell lines for research and diagnostic goals. Production of hybridomas that produce therapeutic antibodies can be accommodated upon demand.

3. Establishment of a repository for animal cell lines and hybridomas of interest to the medical, agricultural, pharmaceutical and research community in Jordan and neighbouring countries.

#### Whom do MONOJO serve?

Hospitals and diagnostic laboratories, blood banks, biotechnology firms and research centres in Jordan and overseas are our potential customers.

[Ref: http://www.ncb.gov.jo/content/msgFromDirector.htm]



Anouncement

### 11<sup>th</sup> Iranian Pharmaceutical Sciences Conference (IPSC2008)

#### 18-21 August, 2008, Kerman, Iran

Aug 18, 2008, Morning: Conference Registration, International Centre for Science & High Technology & Environmental Sciences, Kerman, Iran

First of all you should make your registration through "online registration" pathway, and then you should log in the site by typing your ID and password. After login process, "Payment" and "Abstract Submission" links will be accessible and you can pay your payment and submit your abstract via the links of congress website.

Web address: http://www.ipsc2008.ir/ Secretariat: Tel: +98 341 3205201 – 2 Fax: +98 341 3205203 Address: Haftbagh-alavi Highway, Kerman, Iran P.O.Box: 76175-493





### **Cover pictures**

### **Cover Pictures Description (up to down)**

**Title:** The seven transmembrane α-helix structure of a G-protein-coupled receptor. **Description:** G protein-coupled receptors (GPCRs), also known as seven transmembrane domain receptors, 7TM receptors, heptahelical receptors, and G protein-linked receptors (GPLR), comprise a large protein family of transmembrane receptors that sense molecules outside the cell and activate inside signal transduction pathways and, ultimately, cellular responses. **Source:** http://en.wikipedia.org/wiki/G protein-coupled receptor

**Title:** The diversity of genetic mutations is illustrated by this San Diego beach scene drawn with living bacteria expressing 8 different colours of fluorescent proteins.

**Description:** A San Diego beach scene drawn with an eight colour palette of bacterial colonies expressing fluorescent proteins derived from GFP and the red-fluorescent coral protein dsRed. The colours include BFP, mTFP1, Emerald, Citrine, mOrange, mApple, mCherry and mGrape. Artwork by Nathan Shaner, photography by Paul Steinbach, created in the lab of Roger Tsien. **Source:** http://en.wikipedia.org/wiki/Green\_fluorescent\_protein

**Title:** Immunofluorescence image of the eukaryotic cytoskeleton. Actin filaments are shown in red, microtubules in green, and the nuclei in blue

**Description:** Endothelial cells under the microscope. Nuclei are stained blue with DAPI, microtubules are marked green by an antibody bound to FITC and actin filaments are labelled red with phalloidin bound to TRITC. Bovine pulmonary arthery endothelial cells **Source:** http://en.wikipedia.org/wiki/Antibody

**Title:** 3D model of three types of single-walled carbon nanotubes (Created by Michael Ströck (mstroeck) on February 1, 2006. Released under the GFDL)

**Description:** The potential of multi-functional carbon nanotubes (CNT) for biomedical applications, in particular is to act as magnetic nano-heaters, drug-carrier systems and sensors which allow a diagnostic and therapeutic usage on a cellular level. CNT with tailored functionalities (different filling, heat sensitive caps) will be synthesized and modified to become compatible to biological systems. Studies of their interaction with biological environments (immune response, toxicity, interaction with the single cell) will provide the basis for applying the CNT for imaging (nanoparticles-based contrast agents), sensoring (nanoparticles-based diagnostics) and cancer treatment (hyperthermia, nanotechnology-based targeted drug delivery).

Source: http://en.wikipedia.org/wiki/Carbon\_nanotube

