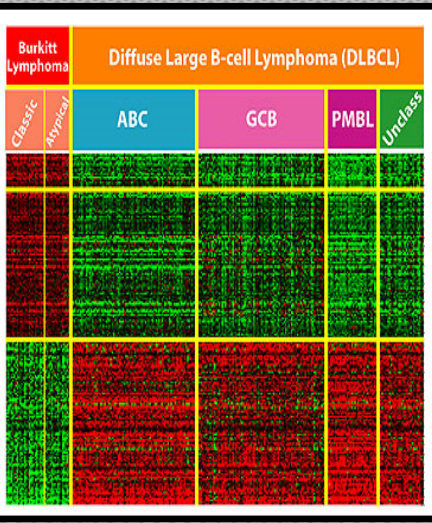

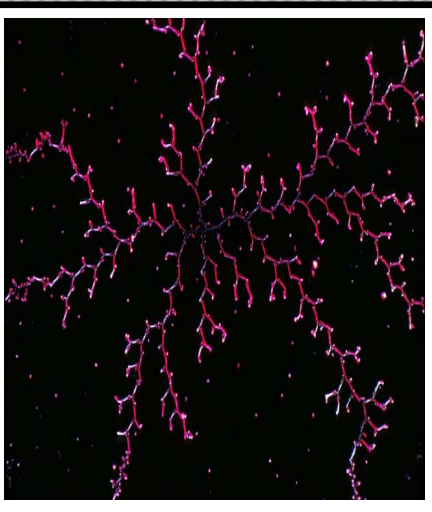

EMHGBN (EMGEN)* Newsletter

Vol. 2, Issue 11, 25th November, 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 steering committee members of the member countries.

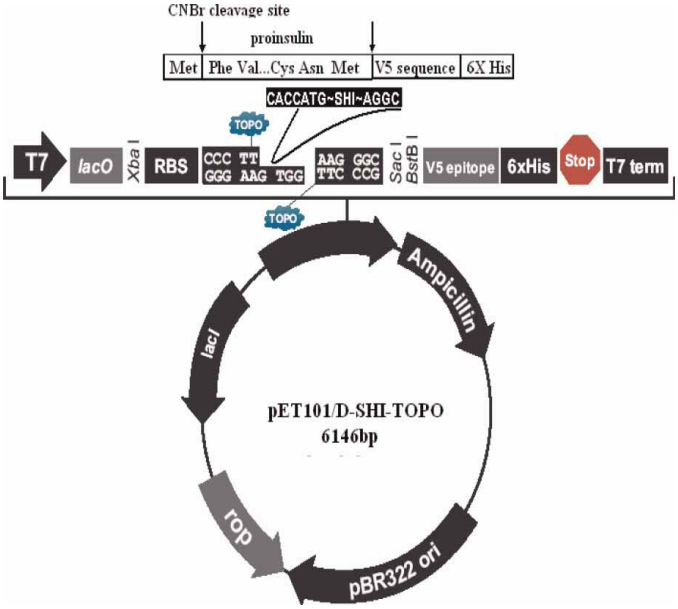
Article

Synthesis of the Human Insulin Gene: Protein Expression, Scaling up and Bioactivity

The article entitled "Synthesis of the human insulin gene: Protein expression, scaling up and bioactivity. Preparative" focuses on development of a synthetic version of human insulin with properties comparable to commercial insulin products in the market. The corresponding author of this article Dr. El-Rashdy M. Redwan is a researcher Bioprocess Technology Departments, Genetic Engineering and biotechnology Research Institute, Mubarak City for Scientific Research and Technology Applications, Alexandria, Egypt. This article has been published in the journal, Preparative Biochemistry and Biotechnology, Volume 38, Issue 1, January 2008.

Dr. El-Rashdy M. Redwan

Diabetes is a major problem worldwide, especially in the Middle East, where eight countries from the region are among the ten countries which have the most diabetes patients worldwide. Initial approach in cloning insulin genes employed by the scientists comprised of inserting the nucleotide sequence coding for the human insulin A and B chains into two different *E. coli* cells. For such an approach synthetic genes offer many advantages over cloned naturally occurring genes, which are associated with problems such as high G C or A T content, codon bias, and complex intron/exon structures. Such problems can be overcome with the use of a synthetic gene, this way the protein coding sequence can be directly optimized for the expression system of choice. An appealing variant of such method is assembling PCSR, which involves generating overlapping oligonucleotides. When assembled, these form the template for the gene of interest. The oligonucleotides are then amplified

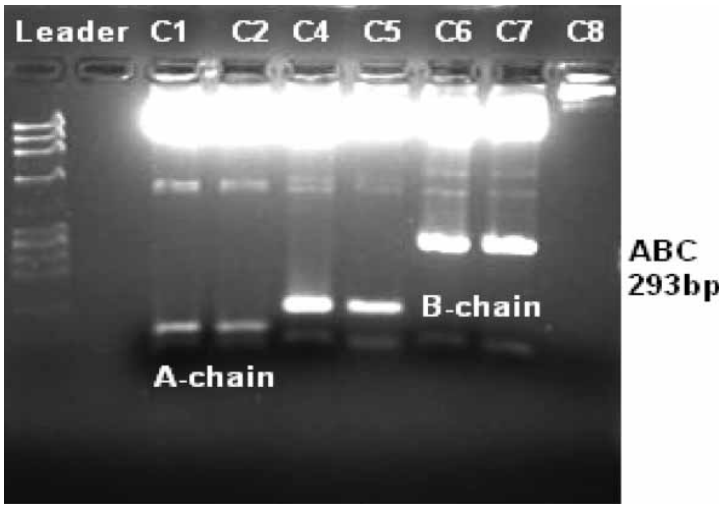


Representative digrams showing the pE101 expression vector components and insulin inert between TOPO cloning site (directional) which was complementary with the flanked ends of the amplified insulin gene to be under the T7 promoter, and yielded 6146 bp. The construct added into the pro insulin produced a peptide at the C-terminal of 3 KDa. The arrow points at the chemical cleavage sites.

and extended by PCR to assemble the full-length gene in a single step.

In this study, Human pro insulin gene of 293 bp was synthesized using a battery of overlapped synthetic oligonucleotides, then cloned into pET101directional TOPO expression vector downstream to the T7 promoter. The pro insulin products were produced as inclusion bodies in *E. coli* at a level of 10%. The batch cultivation of the strain yielded 6 g/L, while the high cell density of fed-batch cultivation yielded 46 g/L. The pro insulin purification yielded 110 mg/gram cell weight, and 1.3 mg/gram of a bioactive insulin. The native insulin was generated by enzymatic conversion of chemically processed pro insulin.

The produced insulin and commercial insulins were compared using variety of methods. SDS-urea-PAGE (Mini Vertical Gel Unit, Invitrogen) was employed to follow the insulin expression in all non-induced cultures, induced cultures and the different steps of protein purification in comparison to its commercial version. Additional analytical analysis for processed insulin was performed using ELISA, dot-ELISA, Western blot, and bioassay and RF-HPLC. The result indicated the potential bio-effect of processed insulin in comparison with that of commercial insulin. The results of the current study indicate two steps: gene synthesis and direct expression can be used to produce native insulin. The reasonable level of expression, refolding, and then enzymatic conversion of the pro insulin into functionally active native insulin makes this production process quicker and favourable in comparison to traditional methods. The processed insulin matched the commercial version in molecular weight, immunological assays, and in vivo bioactivity. A great difference in the value of biomass produced by the fed-batch technique was remarkable. This fermentation procedure yielded a final mass weight of 46 g per liter over a 43 h period. In fed batch, the fermentor biomass was 6-fold higher than the batch process, while it was 7.6-fold higher than the shake flask value.



Fingerprint of ligated vector: insert. 2% agarose gel showing A, B, and ABC chain fragments digested from pET101D. SHI vector. C1, C2 indicate into A chain of 75 bp, C4, C5 indicate into B chain of 105 bp, and C6, C7 indicate the ABC chains of human insulin of 293 bp, while C8 the vector without insert. Both B and A chains are not presented in this study.

New Targets for Antibacterial Agents

The article entitled "New Targets for Antibacterial Agents" describes variety of techniques for discovery of new antibacterial target. This study was carried out by Fatma Abdelaziz Amer, Eman Mohamed El-Behedy and Heba Ali Mohtady. The corresponding author of this article, Prof. Fatma Amer, currently conducts research at the Microbiology and Immunology Department, Faculty of Medicine, Zagazig University, Zagazig, Egypt. This article was published in the journal, Biotechnology and Molecular Biology Reviews, Volume 3, Issue 3, June 2008.

Prof. Fatma Abdelaziz Amer

Associate Prof. Heba Mohtady

The alarming increase of bacterial antibiotic resistance is one of the most serious problems in healthcare worldwide. Thus, the search for new antibacterials directed toward new targets is not only a continuous process but also, at this time, an urgent necessity.

Recent advances in molecular biological technologies have significantly increased the ability to discover new antibacterial targets and quickly predict their spectrum and selectivity. Many essential bacterial proteins have been identified as potential drug targets. However, an ideal target is recognized as that different from existing targets, essential for microbial cell survival, highly conserved in a clinically relevant spectrum of species, absent or radically different in man, easy to assay, and has a well understood biochemistry. The most extensively evaluated bacterial targets are: quorum sensor biosynthesis; the two component signal transduction (TCST) systems; bacteria division machinery; the shikimate pathway; isoprenoid biosynthesis and fatty acid biosynthesis.

Quorum Sensing (QS) System is based on the interaction of signal molecules [autoinducers (AIS)], sensor kinase and response regulator, to activate or repress gene expression. QS inhibitor or blocking strategies include blocking of AIS synthesis, blockade of their receptor site or their processing, or their degradation. Combination of mechanisms would be expected to be more effective. QS systems are also important determinants when bacteria grow in biofilms. A very important clinical requirement is to block biosynthesis of the quorum signalers that initiate biofilm development. Two antibacterial groups inhibiting biofilm formation in *P. aeruginosa* by targeting QS system are: anthranilate analog (methyl anthranilate) and synthetic furanone.

TCST systems consist of a receptor histidine kinase (HK), which reacts to an extracellular signal by phosphorylating a cytoplasmic response regulator, causing a change in cellular behavior. The most common inhibitors reported to date are compounds inhibiting HK.

Bacterial division machinery comprises a set of essential proteins. They include FtsZ, FtsA, ZipA, FtsK, FtsQ, FtsL, FtsW, FtsI, FtsN and others. FtsZ protein, FtsA protein, FtsA-Ftsz interaction, FtsZ-ZipA interaction are considered promising targets.

The shikimic acid pathway effects the conversion of two simple products of carbohydrate metabolism into the chorismate. Chorismate represents a major bifurcation point of the pathway and is a common non-aromatic precursor for the biosynthesis of a range of aromatic metabolites. The components of this pathway constitute excellent drug targets. Examples are: shikimic acid, shikimate kinase, 5-enolpyruvyl-shikimate-3-phosphate synthase and chorismate synthase.

Isoprenoids (lipids) synthesis is a prerequisite for many vital processes. Isopentenyl diphosphate and dimethylallyl diphosphate serve as the universal precursors for their biosynthesis, which occurs by either the classical mevalonate pathway, or non-mevalonate pathway. Whereas, eukaryotes, archaea, Gram-positive cocci, *B. burgdorferi* and *C. burnetii* employ exclusively the mevalonate pathway, many Gram-negative bacteria and apicoplast type protozoa including the *Plasmodium* spp. utilize the non-mevalonate pathway.

The mevalonate pathway enzymes in Gram-positive cocci are of particular interest in the light of the recent development of multidrug-resistant strains. Meanwhile, the distribution of the non-mevalonate pathway makes it an attractive target for the design of antibiotics against pathogenic bacteria and the malaria parasite *P. falciparum.*

Fatty acid biosynthesis comprises a repeated cycle of reactions involving the condensation, reduction, dehydration, and subsequent reduction of carbon-carbon bonds. FAS occur by type I pathways in eukaryotes, and type II pathway in bacteria and *P. falciparum*.

Most of the FASII enzymes are suitable targets for antibacterial drug discovery. Reductases are receiving the greatest attention as one of the most attractive antibacterial targets. FabI, the enoyl-ACP reductase, is one of the most intensively explored pathway targets. FabI inhibitors are extremely potent against many important pathogens, such as multidrug-resistant *S. aureus.* Clinically useful drugs against it are likely to arise.

Perhaps a wealth of new validated targets for progression through the antibiotic drug discovery process is available. New antibiotic leads are being identified. The current challenge is to optimize these early-stage discovery which leads to make them suitable for clinical evaluation.

RNA interference and its Potential Applications in Research and Healthcare

Introduction

RNA interference (RNAi) is one of the most outstanding recent discoveries in the field of genetics. The discovery of RNAi came about accidentally when the anti-sense strand of *par-1* gene of the nematode *C. elegans* was injected to the organism in order to block the expression of the gene. During the following experiments it was observed that the sense strand also suppresses the expression of the gene. Later it was discovered that double-stranded RNA (dsRNA) results in much more efficient gene silencing. The basic mechanism of this process has been significantly clarified through various *in vitro* and *in vivo* studies. The process is initiated by presence of dsRNA in cytoplasm; dsRNA is not a requirement for production of normal gene expression but is produced (at least transiently) by many viruses. dsRNA strands are cut into 21–23 nucleotide pieces by the dicer nuclease, a dsRNA specific endonuclease which is a member of the RNAase III family of nucleases. The resulting silencing inducing RNAs (siRNA) are then incorporated into RNA induced silencing complex (RISC). The produced siRNAs contain two perfectly complementary strands of RNA; they guide the RISC to the target RNA, which is then cleaved in the middle of the target region and hence degraded.

Recent findings demonstrate that dsRNA can trigger gene silencing through at least four different mechanisms. It was first established that RNAi induces mRNA destruction as mentioned earlier. Also RNAi-related mechanisms have been shown to have effect on chromatin structure resulting in transcriptional suppression of the targeted genes. Furthermore a mechanism involving RNAi can direct *de novo* methylation of genomic DNA leading to transcriptional suppression of the targeted genes. An RNAi-related mechanism functions by inhibition of mRNA translation of targeted genes. In addition in certain protozoa, small RNAs are able to conduct chromosomal rearrangement through RNAi-related mechanisms.

A clear role RNAi gene silencing is to block abnormal and unwanted gene expression resulting from viruses, transposons and transgenes. The best-understood role for RNAi gene silencing is as a part of the systemic antiviral response in plants. Viral RNAs can be targeted by RNAi gene silencing mechanism. RNAi silencing mechanism can then generate silencing signals with sequence-specific information that spread from cell-to-cell through plasmodesmata and through the vascular system to different organs of the plant.

Applications

Gene Function Analysis

RNAi is a promising technology for functional analysis of the genome of rat and mouse. The silencing effect obtained by transferring mice with RNAi constructs is stably passed through germline. Using this approach variety of silencing effects can be achieved; from silencing specific splice variants of a gene to silencing whole gene families. RNAi can also be helpful in overcoming the difficulty of creating double-knockout mutants of mouse, where the two genes have loci in close proximity.

Using RNAi, new types of experiments can be conducted in mammalian systems. For instance gene expression can be altered spatially and temporally to determine the amount of gene products required for specific processes at particular stages of development. To achieve this, siRNA producing virus or plasmid can be injected or electroporated locally. Such an approach can overcome the difficulties of traditional techniques in finding regulatory regions that can express recombinase proteins in the desired patterns.

Genomic Screening

In mammalian cell cultures, RNAi effects can be induces by delivery of siRNA or stable expression of small hairpin RNA, (shRNA) which is processed to siRNA inside the cells. Loss-of-function genetic screens can be performed in cultured cells using libraries of shRNA. Many large-scale genome screens have been performed in mammalian cell cultures. These screens have identified genes involved in apoptosis, signaling, regulation of protein stability and the ultraviolet radiation damage response. Today RNAi has become the ideal approach for functional genomics analysis in mammalian tissue culture. Several factors contribute to this, including high gene-silencing rate achieved at low concentrations of the transgene RNAi, ease of finding accessible target sites, high specificity, good stability and availability of custom RNAi at comparatively low cost.

However in many biological processes there are genes involved that cannot be studied in cell culture context. Therefore there have been efforts to use RNAi technology in whole model organisms such as mouse. Transgenic RNAi mice have been produced for this purpose. This can be achieved in two ways. In first approach embryonic stem (ES) cells are transferred with RNAi constructs followed by production of whole organism using the ES cells. Alternatively one-cell embryos can be infected or injected with lentiviruses carrying appropriate shRNA sequences. Such a method has been successfully employed for identification of genes important to kidney function in mouse.

In conventional knockout approaches, the produced mutant allele is null. This can be a great tool in determining the gene function, but it is not always the most useful, especially when the loss of function of the targeted gene proves to be lethal at the early embryonic stages. Transgenic RNAi can act as hypomorphic allele. Using transgenic RNAi one can produce a number of transgenic lines with different degrees of loss of expression/function, thus overcoming the problem of null allele in traditional knockout approaches.

In addition, several near genome- wide RNAi screens have been conducted using long dsRNA in *C. elegans* and *Drosophila melanogaster*, identifying genes involved in processes such as cell division, apoptosis and cell morphology.

Despite being relatively fast and cheap, RNAi screening has several disadvantages when compared with conventional screening methods. Conventional methods can produce dominant-negative as well as gain-of-function mutations, which are sometimes essential for understanding the gene function. Furthermore using the conventional methods one can identify mutations outside the coding region. In RNAi screening, siRNAs never fully suppress the targeted gene and often many siRNA need to be screened in order to identify a siRNA with enough efficacy. In rapidly dividing cultured cells, transient RNAi last three to five days. Even in slowly dividing cells, an effective siRNA might have difficulty suppressing a stable protein. Also, different cell types can have varying amount of available RISC which would further limit the effectiveness of RNAi.

Therapeutic Potentials

RNAi has various therapeutic potentials. Now days, the genetic basis of many disorders have been identified, and as mentioned earlier, targeted by RNAi in *in vitro* and *in vivo* model systems. Because of the high specificity of RNAi, its most obvious therapeutic use would be in disorders in which polymorphism within the disease-inducing gene, in a certain group of cells, such as a tumor, can be targeted for degradation without affecting RNA from wild-type alleles. In humans many disorders, especially cancer are caused by mutations and rearrangements that can be treated in such a way. The fact that siRNA are natural products of the cell may indicate that they do not result in production of toxic compounds.

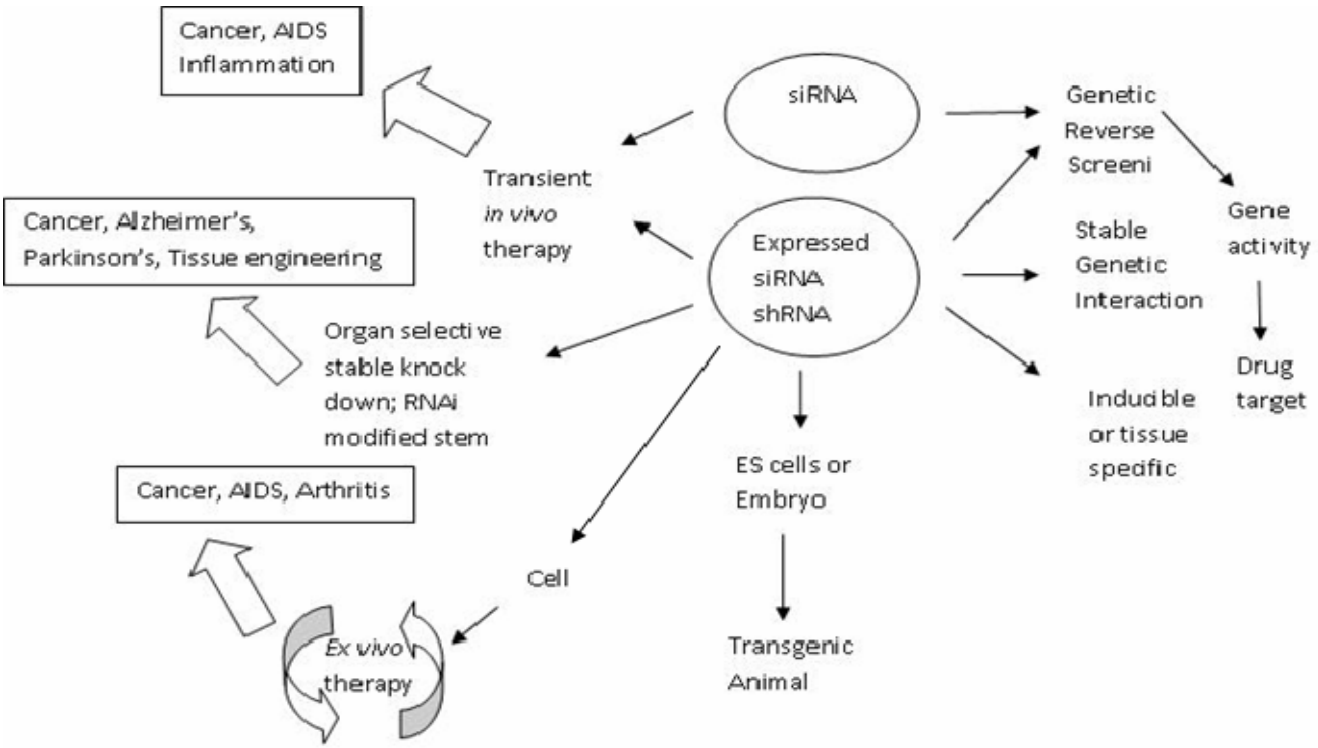
RNAi and Cancer Therapy

In order to use RNAi for cancer therapy, efficient and stable expression of the RNAi sequences need to be achieved. For this reason many researchers have cloned the RNAi expressing sequences into many viral vectors.

It has been experimentally shown that intratumoral injection of an adenovirus carrying the siRNA targeting the hypoxia-inducible factor-1 (HIF-1). HIF-1 has a considerable effect on tumor growth when combined with radiation therapy.

The translocation of the Philadelphia chromosome (Ph) generates a fusion gene called *BCR-ABL*. The translation product of this gene creates a constitutively active protein tyrosine kinase that causes leukemic transformation in chronic myelogenous leukemia and Ph-positive acute lymphoblastic leukemia. The siRNAs sequences targeting the *BCR-ABL* transcript have been demonstrated to silence the oncogenic fusion transcripts without affecting expression levels of normal c-ABL and *c-BCR* transcripts.

A major problem in cancer therapy is the resistance of cancer cells to chemothrapeutic agents. *MDR1* gene is a multidrug transporter that has a major role in multidrug resistance. RNAi has been shown to be able to decrease the resistance of cancer cells *in vitro* by silencing the *MDR1* gene.



Some potential applications of RNAi gene silencing; both externally applied siRNA and expressed siRNA and shRNA can have significant applications as therapeutic and research tools.

Most current approaches in RNAi cancer therapy employ traditional gene therapy delivery systems, which deliver siRNAs locally. However cancer is a systemic disease and includes metastatic distribution of cancer cells and hence for RNAi technologies to be effective, a systemic delivery approach is required. Development of systemic delivery methods for RNAi would enable

using tissue-specific or cell-specific gene promoter vector or specific antibody-conjugated carriers, hence reduce the amount of RNAi required and hence would decrease the associated side-effects.

RNAi in Treatment of Infectious Diseases

The greatest potential therapeutic application of RNA is in treating infectious diseases. The exogenous origin of the targeted RNA, enables silencing of the pathogen RNA without affecting the cellular functions. Another approach would be to target cellular transcripts that that whose products are essential to virulence of the pathogens. In the case of viruses with RNA genome, there is possibility to directly target the viral chromosome, thus enabling the prevention of establishment of virus in the cells, thereby sterilizing the cell even after infection.

RNAi presents an attractive opportunity for treating the Human Immuno-deficiency Virus (HIV). It has been show in cell culture models that RNAi targeted at HIV genome can significantly reduce the virus production inside the cells. Also, RNAi targeted at the major HIV receptor protein, CD4, results in decreased entry of virus into cells. It has been shown that specific siRNA applied to human cells from the outside, in same manner as a drug, could enter them and protect them against infection by rapidly multiplying poliovirus. These studies showed that if the siRNA were expressed from inside cells, rather than simply delivered from the outside, the cells became largely immune to subsequent HIV-1 infections. Furthermore, effectiveness of RNAi therapy has been demonstrated in treatment of Hepatitis C Virus (HCV), Hepatitis B Virus (HBV), sepsis, neurodegeneration and other disorders.

Future Directions

Using plasmid and viral vectors RNAi can be delivered in a stable and long-term fashion. However it is unlikely that this would be established as a standard therapeutic method. Apart from the dangers associated with using vectors that integrate into the genome, expression of RNAi might results in harmful effects in target organism. New cellular processes involving RNAi are being discovered and RNAi administrated as therapeutic agents might have unwanted effects on such mechanism. For instance, an excess of a virus-specific siRNA in the cell might saturate RNAi mechanism and lead to interruption of the pathway's normal functions in the cell.

Despite the technical challenges, RNAi-based technologies offer significant advantages over the traditional gene silencing techniques. RNAi is a relatively new discovery and further research in this field might significantly contribute toward understanding of gene regulations. Regarding treatment of viral disease as well as cancers, there is a great need for therapeutic agents that are sequence-specific and can cope with high rates of mutation. As such, it is reasonable to expect the emergence of RNAi-based therapeutics in near future.

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Princess Haya Biotechnology Center

A Brief Description of the Center

The Princess Haya Biotechnology Center was established at the Jordan University of Science and Technology on the campus of King Abdullah University Hospital in 2003.

Since its establishment, the princess Haya Biotechnology Center has been a pillar of the scientific activity in Jordan through the cooperation agreements with the local institutions and hospitals dealing with genetic diseases in Jordan and through the continuous scientific activities at the national and regional levels. For instance, the center coordinates and cooperates with the Jordanian organization for the cystic fibrosis, the Jordanian organization for the Down syndrome and the thalasemia center at Princess Rahma Teaching Hospital in Irbid. Recently and as part of its policy to transfer expertise and biotechnologies through continuous education programs, the center hosted a workshop in cooperation with the Red Cross on forensic medicine and its applications. Another workshop on the latest advances in the area of protein technology was hosted in cooperation with the international BioRad Corporation. Furthermore, the center actively seeks to advance the pharmaceutical industry in Jordan through its R&D cooperation agreements with the national pharmaceutical companies. In accordance with its mission to advance scientific knowledge, the center hosts students from other Jordanian universities to introduce them to the latest research techniques employed by the center.

The center aims to increase awareness of the importance of biotechnology and research in order to help solve the large number of medical and health problems suffered by Jordanian people. In addition, the center seeks to actively participate in creating an advanced biotech industry on a firm scientific and technological base. For this reason the center has the short term goal for this year of preparing an Oracle database that should become a nucleus for the most advanced center for biotechnology and bioinformatics in the Arab region and will help the center achieve its long term goals. In addition, the center hopes to establish a virology research unit this year in light of the pressing need for such a unit in the kingdom created by the recent rise of incidents in of the Bird Flu and other viral infections in adjacent countries.

Collaborations

- The forensic medicine institute in Iraq
- The Saint Joseph University in Lebanon
- The Hamdan Bin Rashid Organization for Excellence in the UAE
- Human Genetics Center at the University of Humboldt in Germany
- The Forensic Medicine Center at the University of Western Australia

Facilities

The center has provided faculty members and graduate students from different disciplines at the university with an excellent, unprecedented infrastructure for experimental research in biotechnology, especially in the fields of genomics and proteomics. Currently, approximately twenty graduate students working towards the Master's degree are conducting research at the center under the supervision of a distinguished group of faculty members from the colleges of Medicine, Science, Medical sciences, Dentistry, and Agricultural Sciences.

The center houses sixteen research laboratories, and occupies approximately 1500 square meters. It is managed by a staff of four employees and seventeen distinguished technicians holding the bachelor's and Master's degrees.

Research Activity

Genomic Research Group

The genomics facility in Princess Haya Biotechnology Center provides access to advanced technologies that are beyond the reach of virtually any individual laboratory in the region. The facility is well equipped with state-of –the-art instrumentation that includes two ABI Prism 310 Genetic Analyzers purchased from Applied Biosystems Corporation, USA. This is an automated single-capillary genetic analyzer designed for a wide range of DNA sequencing and fragment analysis applications including comparative sequencing, linkage analysis, SNP detection, mutation detection, discovery and validation of base -pair changes in sequence, a range of forensic DNA applications and variety of other applications. DNA sequencing is performed on double stranded, PCR generated DNA and plasmid templates. Sequencing reactions are performed using the Applied Biosystems Big Dye Terminator V.3.1 and V.1.1 chemistries.

Amplification of specific DNA sequences is carried out using the BioRad iCycler. Qiagen plasmid DNA preparation kits are used to purify plasmid DNA samples and PCR products are commonly purified using Qiagen kits (i.e. QIAquick) and assessed using the latest BioRad electrophoresis units. Mutations detection is one of our key strengths in the center. The BioRad DeCode universal mutation Detection system is commonly used for the screening of the mutation within specific gene including both SSCP and DGGE techniques. The facility also carries out gene-scan and variety of STRs-based applications including paternity and identity testing using the 16 loci identifier kit supplied by Applied Biosystems. STRs-base linkage studies are also performed on a number of genetic diseases such as β-thalassemia, cystic fibrosis and familial Mediterranean fever**.**

Also the center has Real-Time PCR (Stratagene MX-4000, USA). This unit offers the center the ability to perform sensitive, accurate and reproducible measurements of levels of gene expression. The machine can be used for a wide variety of applications including measurements of viral load, performing allelic discrimination studies, SNP analysis, mutational analysis, detection of chromosomal translocations and detecting mRNA splice variants. The open format of this machine allows researchers to work with a variety of fluorogenic probe systems such as Taq-man, molecular beacons and SYBR-Green probes. Currently, the Real-Time PCR is used for the quantitation and genotyping of infectious diseases such as, Hepatitis B, C and Cytomegalovirus and for mutation detection for different genetic disorders.

Metabolomics Research Group

The metabolomics laboratory in Princess Haya Biotechnology Center (PHBC) in Jordan University of Science and Technology (JUST) and located in King Abdullah University Hospital (KAUH) is committed to the diagnosis, Training and research of inherited metabolic disorders, particularly those affecting the metabolism of branched-chain amino acids, fatty acids, glycogen, fructose, minerals and the urea cycle. It has recently been consolidated the laboratory services into a single facility that offers a wide range of sophisticated metabolite evaluation and profiling testing pertinent to the diagnosis of inborn errors of metabolism.

Therapeutic Drug Monitoring Research Group

Therapeutic drug monitoring (TDM) can be defined as the use of drug measurement in biological fluids as an aid to the management of patients receiving drug therapy for the alleviation or prevention of diseases. TDM in several centers remains within the confines of clinical biochemistry departments that provides only the measuring (assay only) and not the monitoring (assay and clinical interpretation) service.

Clinician routinely monitor drug pharmacodynamics by directly measuring physiological indices of therapeutic response e.g. lipid concentration, blood glucose, blood pressure or clotting tests. For many drugs there is either no readily available measure of effect or it is insufficiently sensitive. Large interindividual variation in the relationship between dose and response can make individualizing drug dosage difficult, for example drugs with narrow therapeutic indices, large interindividual variation in pharmacokinetics, or concentration dependent pharmacokinetics. Other

cases it is difficult to distinguish between the progress of the disease and the pharmacological effects of a drug. It is in these situations that TDM is an essential part of clinical management.

Proteomics Research Group

The proteomics core facility combines in-depth expertise with state-of-the-art facilities for the large-scale characterization of proteins expressed in health and disease. The goal is to identify protein structures, interactions and pathways so that new disease markers and drug targets can be identified that will help create new products to prevent, diagnose and treat diseases. Furthermore, the center is providing the local pharmaceutical industry with the technical expertise and equipments necessary for the quantitative analyses of drugs, steroid and peptide hormones, vitamins, eicosanoids, proteins, lipids, and enzymes. The staff has experience in all facets of proteomics analysis including sample processing for high-resolution 2D gel electrophoresis, multidimensional chromatography, mass spectrometry analysis by LC/MS/MS and sequence analysis. The proteomics and mass spectrometry services at Princess Haya Biotechnology Center are accessible to clients from academic institutions as well as industry. Protein and peptide purification through chromatography, 1D and 2D gel electrophoresis, gel imaging and analysis, sample processing (i.e., enzymatic digestion and fractionation), peptide mass fingerprint (PMF) through LC-MS/MS approaches and protein identification are offered. The staff is always looking for the development and implementation of new and innovative approaches in the study of various research problems.

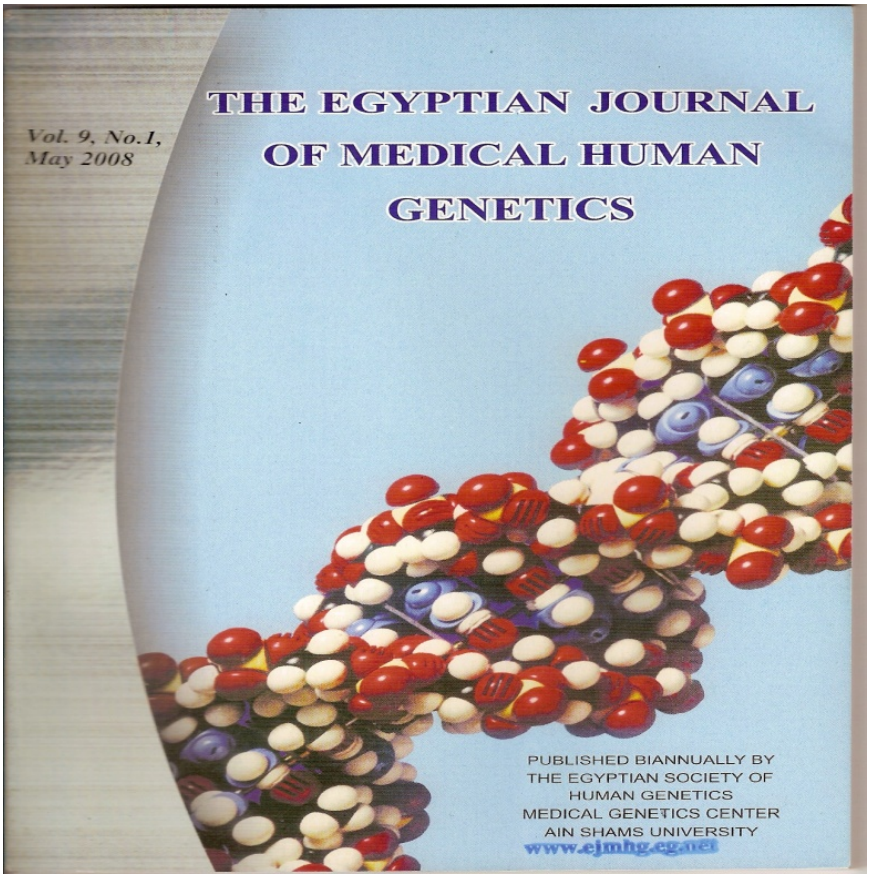
Current Research

- Screening for human Heparan Sulfate proteoglycan gene mutations associated with Familial Schwartz Jampel Syndrome among Jordanian families.
- Screening for *ATP1A2* gene mutations Associated with Familial Hemiplegic among Jordanian families.
- Screening for beta globin gene mutations Associated with β-thalassemia in Jordanian families.
- Screening for *SERPING1* gene mutations Associated with Angioedema in Jordanian families.
- Screening for *SPINK5* gene mutations Associated with Netherton Syndrome among Jordanian families.
- Screening for *FBN1* gene mutations Associated with Marfan Syndrome among Jordanian families.

Reference: http://www.just.edu.jo/CENTER/PHBC/

Announcement

The Egyptian Journal of Human Medical Genetics



Cover Pictures Description (From top to bottom)

Title: Multicolor corn
Description: Pictured is an ear of corn, the kernels are varied in colour. Researchers suggest that retroviruses have additional stretches of DNA that act as switches, turning on genes when inserted next to them in the cell's chromosomes. Similar activation of genes causes the variation in pigmentation of these corn kernels.
Source: Created by Linda Bartlett at national cancer institute, U.S.A, 1980.
http://visualsonline.Cancer.gov/details.cfm Image # AV-8000-0341

Title: Technology: Microarray
Description: DNA-microarray analysis of Burkitt's lymphoma and diffuse large B-cell lymphoma (DLBCL) showing differences in gene expression patterns. Colors indicate levels of expression; green indicates genes that are overexpressed in normal cells compared to lymphoma cells and red indicates genes that are overexpressed in lymphoma cells compared to normal cells.
Source: Created by Louis M. Staudt, Found at Molecular Diagnosis of Burkitt's Lymphoma, New England Journal of Medicine, June 8, 2006, Vol. 354 (23), 2431-2442.
http://visualsonline.cancer.gov/details.cfm Image # 4155

Title: Treatment: Drugs: Cisplatin
Description: The image shows cisplatin crystals, which is a platinum compound, and used as a chemotherapy drug.
Source: Created by Larry Ostby, National cancer institute, U.S.A, 1987.
http://Visualsonline.cancer.gov/details.cfm Image # AV-8712-3464-D