

# EMHGBN (EMGEN)\* Newsletter

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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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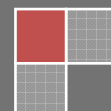
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EMGEN is a shortened form of EMHGBN that was approved for the ease of use.

## Lack of Evidence for Complete Resistance of Peripheral Blood Mononuclear Cells to HIV-1 and HIV-2 Infection

*The article entitled "Lack of Evidence for Complete Resistance of Peripheral Blood Mononuclear Cells to HIV-1 and HIV-2 Infection" aims to investigate whether certain peripheral blood mononuclear cells (PBMCs) are completely resistant to HIV-1 and HIV-2 infection or not through in vitro techniques. The study was done by Dr. Ali A. Al-Jabri, R. Lambkin and J.S. Oxford. Corresponding author of this paper, Dr. Ali Al-Jabri is working in the Immunology Unit, Department of Microbiology and Immunology, College of Medicine and Health Sciences Sultan Qaboos University, Muscat, Oman and the paper was published in Viral Immunology. 2008 March; 21 (1): 83-90.*

People differ in their susceptibility to infection with HIV-1 and some infected individuals progress faster than others towards the terminal stages of the disease. In particular, it has been observed that some regular sexual partners of HIV-1 sero-positive patients and some children born from infected mothers show no clinical or serological signs of infection. This has raised the question that whether some individuals are completely resistant to or protected from HIV infection.

Peripheral blood mononuclear cells (PBMCs) obtained from healthy donors, when infected *in vitro* with HIV-1, differ in their susceptibility with those showing relative resistance to infection. In this study we have investigated, using a relatively large number of PBMCs obtained from different individuals, whether some PBMCs are completely resistant to either HIV-1 or HIV-2 infection, under carefully controlled *in-vitro* conditions.



Dr. Ali A. Al-Jabri

Sultan Qaboos University, Muscat,  
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Evidence for acquired resistance to HIV infection may reflect previous immunological priming with a low sub-infective dose of virus. Individuals who appear to be naturally protected against HIV infection or from disease progression could be intrinsically resistant through genetic host factors such as genes coding for co-receptors e.g. CCR5 and their HLA genotypes.

AIDS pathogenesis would appear to involve multigene systems such as the HLA complex and the derivative immune response genes of the T cell receptor (TCR). These and other cofactors, such as psychosocial factors and nutrition, are believed to influence disease progression. Differences among PBMCs to support the replication of HIVs have been shown by other studies.

Virus replication was measured using the viral p24 core antigen levels in the case of HIV-1 and by reverse transcriptase (RT) activity in case of HIV-2 at 5, 14 and 21 days post infection.

Our results on p24 core antigen levels for PBMCs from different donors showed considerable variation. Both HIV-1 and HIV-2 isolates showed different patterns of viral replication in PBMC cultures from different donors. Certain PBMCs showed no detectable levels of viral p24 antigen during the 21 days in culture. However, when further tested using a more sensitive ELISA, these PBMCs showed detectable viral replication although some at extremely low levels. Those PBMCs showing extremely low levels of p24 antigen were again re-tested to rule out false positives. All cultures were positive for viral p24 antigen. Moreover, no single individual's PBMC showed complete absence of viral RT activity over the 21 days post-infection period, indicating that none of the tested PBMCs proved to be completely resistant to virus infection or viral replication. In addition, no particular PBMC from a single individual was found to be partially resistance to all 4 viruses tested, although some were shown to be partially resistance to more than one virus.

To investigate reproducibility of the *in-vitro* infectivity testing, PBMCs from randomly selected individuals were tested again. Reproducibility of results was achieved as measured by p24 and RT assays. Taking the values of the original infected cells as 100%, the score in the replicative cultures varied within an acceptable range of  $\pm 8\%$ .

The cohort showed a normal distribution of RT and p24 levels. The score was determined relative to the maximal (peak) RT or p24 levels obtained during the culture period for a particular isolate (at day 21 post infection). According to the defined ranking methodology, 33% of donors showed low replication to infection with HIV-2s (ROD and CBL-20) and a lower percentage (20%) of donors showed low replication to infection with HIV-1s. Additionally 11% of the donors were high for HIV-1 replication and 1.5% high for HIV-2. By excluding high and low groups, 69% and 65.5% of donors showed HIV-1 and HIV-2 production, respectively, as average for the entire cohort. Our results clearly distinguished three groups of PBMCs with varying degrees of viral replication, (a) those able to replicate virus highly, (b) those PBMCs that were moderately productive and (c), those which poorly replicated virus.

This would appear to reproduce *in vivo* observations made of HIV-1 sero-positive patients and their variable rate of progression to AIDS. In the present study, we demonstrated that the rates of HIV-1 & 2 productions *in vitro* vary greatly among individuals, even when other variables such as the degree of lymphocyte activation and culture conditions are carefully controlled. Quantitative differences in virus production can differ by  $>3000$  fold between the highest and the lowest virus producers. Both host cellular factors and viral properties may influence the level of viral replication in any given virus-cell combination.

High and low producers, in the case of HIV-1, can be predicted from the examination of how the HLA-B locus, present in the individual, binds the gp120 peptide of HIV in comparison with the binding of HLA-DR beta chain peptide fragment. It has been assumed that the mimicry of HLA by HIV may theoretically provide the T-cell activation essential for virus replication.

## Evaluation of Renal Gene Expression of Protein Kinase C (PKC) Isoforms in Glomerular Diseases

*The article entitled "Evaluation of renal gene expression of protein kinase C (PKC) isoforms in Glomerular Diseases" aims to evaluate renal expression and the role of two PKC isoforms alpha and Beta in renal biopsies from patients suffering from different Glomerular diseases. The study was done by Dr. Salwa Ibrhim, Laila Rashed and Sawsan Fadda. Corresponding author of this paper, Dr. Salwa Ibrahim is working in the Department of Internal Medicine, Cairo University, Egypt and the paper was published in Scientific World Journal. 2008 Aug, 8: 835-844.*

Hyperglycemia causes glomerular dysfunction through activation of protein kinase C (PKC) extracellular-regulated protein kinase (ERK) pathway enhanced polyol pathway, oxidative stress, overproduction of advanced glycation end products and enhanced growth factors and cytokine production. The inappropriate activation of PKC has been implicated as a putative mediator in the pathogenesis of diabetic nephropathy based on both experimental animal models of type 1 diabetes and studies in cultured glomerular cells. An increase *de novo* synthesis of diacylglycerol (DAG) generated from glycolytic intermediates results in activation of PKC with induction of mesangial and glomerular dysfunction.



Dr. Salwa Ibrahim

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However, PKC is not a single entity but consists of a family of at least 12 serine-threonine kinases with distinct expression patterns and cellular function. These isoforms have been divided on the basis of their regulatory domains into three larger subgroups. Specific PKC isoforms are activated by hyperglycemia and the pattern of activation varies across tissues and cell types. In addition, several PKC isoforms could be involved in diabetes induced organ damage. Evaluation of PKC isoform activation pattern in diabetic nephropathy has gained great interest recently since specific PKC isoform inhibitors have been developed by several pharmaceutical companies. Emerging role for PKC isoforms in immune cell function has been identified recently.

Data on renal PKC isoforms expression in diabetic and nondiabetic glomerular diseases in human are scarce; therefore we conducted this study to evaluate the renal gene expression of classical PKC isoforms ( $\alpha$  &  $\beta$ ) in patients with diabetic nephropathy as well as patients with proliferative glomerulonephritis including lupus nephritis. We also examined the correlation between PKC gene expression and parameters of renal injury including serum creatinine, estimated glomerular filtration rate (eGFR) and 24-hour urinary protein excretion.



Sixty outpatients were selected based upon renal biopsy findings. They were divided into 3 groups: (1) Patients with type 2 diabetes and proteinuria. (2) Female patients with biopsy proven previously untreated focal or diffuse proliferative lupus nephritis (class 3-4). (3) Patients with biopsy proven previously untreated mesangioproliferative glomerulonephritis. Kidney biopsy samples were frozen at -80C.

The homogenized kidney biopsies were examined for detection of PKC gene expression after total RNA extraction. RNA was reverse transcribed by using oligonucleotide primer. PCR reactions were performed by adding forward and reverse primers of protein kinase alpha and beta genes to the synthesized cDNA.

Patients of lupus nephritis were significantly younger and had significantly higher eGFR compared to diabetic patients with nephropathy ( $P<0.05$ ). Diabetic and Mesangioproliferative GN patients, on the other hand were comparable in age, gender distribution, renal function and degree of proteinuria. Renal expression of PKC  $\alpha$  and  $\beta$  genes were significantly increased in diabetic, lupus nephritis and mesangioproliferative GN patients compared to controls.

Renal expression of PKC  $\alpha$  gene was significantly increased in diabetic patients with nephropathy compared to lupus nephritis (LN) and mesangioproliferative glomerulonephritis (MPGN) patients ( $P<0.05$ ). On the other hand, renal PKC  $\beta$  gene expression was significantly increased in LN and MPGN compared to diabetic glomerulosclerosis ( $P<0.05$ ).

## Conclusion

The PKC  $\alpha$  isoform seems to be an important mediator of glucose-induced glomerular changes including increase in vascular endothelial growth factor (VEGF) and its receptor, loss of heparan sulphate proteoglycans and development of albuminuria. The PKC  $\beta$  isoform, on the other hand, seems to be included in the activation of profibrotic pathway through increased expression of TGF- $\beta$ 1 and connective tissue growth factor (CTGF).

Our two important findings are: Enhanced observed renal gene expression of both PKC isoforms  $\alpha$  and  $\beta$  in diabetic kidney tissues, lupus nephritis and MPGN but in different patterns. PKC  $\alpha$  gene expression was greatly increased compared to that of PKC  $\beta$  gene in diabetic kidneys. The ratio of renal PKC  $\alpha$ /PKC  $\beta$  concentrations was 17.41 in diabetic kidney tissues compared to 4.5 in lupus nephritis and 4.89 in MPGN. Secondly, renal PKC  $\beta$  gene expression was significantly increased in lupus nephritis and MPGN compared to diabetic nephropathy (41.01+14.03 ug/ml and 39.93+16.14 ug/ml vs. 18.20+4.91 ug/ml respectively,  $P<0.05$ ).

A novel finding in the present study was to demonstrate an increased renal expression of PKC  $\beta$  gene in MPGN and lupus nephritis patients compared to diabetic nephropathy group. It was also noted that PKC  $\alpha$  gene was co-expressed also in lupus nephritis and MPGN but to a lesser extent in comparison with diabetic kidney tissues. Taken together, these data suggest a major role for PKC isoforms  $\alpha$  and  $\beta$  in the pathogenesis of proliferative glomerulonephritis including lupus nephritis. This also may suggest a potential therapeutic role for PKC inhibition in treatment of proliferative glomerulonephritis.

The co-expression of these two isoforms in the diabetic kidney tissues observed in the current study explained the advanced glomerular structural and functional changes in this group of diabetic patients.

The renal co-expression of both PKC  $\alpha$  and  $\beta$  genes, with predominant  $\alpha$  isoform expression, in diabetic nephropathy might explain the inconsistent effects of selective PKC  $\beta$  inhibition in type 2 diabetic patients with nephropathy.

## **Protein Chemistry Unit of Biotechnology Research Center Pasteur Institute of Iran**

The Protein Chemistry Unit has been established in 1999. During the first year, amino acid analysis laboratory has been set up for identification of peptides and proteins. Besides, reverse phase HPLC is utilized for analytical protein purification, peptide mapping and assays of recombinant protein and synthetic peptide pharmaceuticals based on international pharmacopeias. Circular dichroism spectrometry has been set up for study of secondary and tertiary structures of proteins in early 2004. Installation of two-dimensional gel electrophoresis laboratory has been completed in April 2004. Equipping of this laboratory was funded by national medical biotechnology network in order to achieve the state of the art technique for the separation of complex protein mixtures as a basic separation methodology for further proteomics study. By availability of mass spectrometry facilities the biomedical proteomics could be completely settled down in the Pasteur institute of Iran.

Dr Behrouz Vaziri (PhD, Assistant Professor) is the head of Protein Chemistry Unit at Institute Pasteur of Iran. In this report, we have interviewed Dr. Vaziri as follow:



Dr. Behrouz Vaziri and Protein  
Chemistry Lab Members

Biotechnology Research Center,  
Pasteur Institute of Iran

**1. Dear Dr. Vaziri could you please briefly introduce yourself and explain your educational status?**

Behrouz Vaziri, born in 1966, Pharm. D., Ph.D.

**2. Could you please tell us what your main research area is?**

Proteomics especially in infectious diseases.

**3. Why did you choose this field of research?**

To define the possible new drug targets by developing the basic knowledge of molecular pathogenesis involved in infectious diseases such as rabies. The powerful capabilities of proteomics for determining the mechanisms of drug resistance in regional infectious diseases such as malaria and tuberculosis and also searching for biomarkers involved in their pathogenesis are the other aspects of this field.

**4. How and where you apply biotechnology or genomic tools in your research?**

There are projects running on *in vitro* and *in vivo* models of rabies infection which use proteomic tools to define the protein expression changes and biochemical pathway alterations caused by this virus. This study is done in collaboration with rabies department of Pasteur Institute of Iran (PII). Protein Chemistry Lab is also involved in searching for the possible serum biomarkers of gastric cancer in collaboration with *Helicobacter pylori* Research Group in PII. We are also collaborating with colleagues from Tehran University of medical science for proteomic studies on drug resistant isolated *Leishmania tropica* strains.

**5. Are there any biotechnology centers in your country?**

There are research centers and production units in public and private sectors.

**6. Are there any academic training courses in Biotechnology in your country? In which level and how many students are trained annually?**

There are universities and research centers for training M.Sc. and Ph.D. students annually. PII has also two established Ph.D. programs in pharmaceutical and medical biotechnology as well as Master courses for Medical Microbiology.

**7. Are you familiar with EMRO countries and EMHGBN (Eastern Mediterranean Health Genomics and Biotechnology Network)? Would you please tell us how you know the EMHGBN?**

Yes. The focal center of EMHGBN is in PII and I already have some workshops on proteomics supported by the team.

**8. What is your opinion about industrial biotechnology and its development in EMRO countries?**

It is absolute need for steady and continuous developing in EMRO countries.

**9. Do you have any suggestions for collaborations with EMRO countries?**

Our facilities for proteomics research based on 2-DE and MS are opened to all researchers interested on medical based proteomics researches.

**10. Do you have any collaboration with biotechnology research centers in EMRO countries?**

Not yet, but already tried to establish one with biotechnology Department of Sultan Qabus university of Oman. Hopefully, we could soon define a fruitful collaboration.



**12. Are there any possibilities for young researchers from EMRO countries to participate in training course in your biotech centers?**

Yes, that is quite possible and we looking forward to it in deed.

**13. Do you have any governmental support for biotechnology in your country?**

Yes, we have.

**14. What kinds of biotechnology facilities do you have in your laboratory and your research center?**

Protein chemistry and proteomics research laboratory is equipped for characterizing of recombinant proteins and also for proteomics research. We have different analytical protein purification systems including HPLC, CE, 2-DE gels and related softwares. Circular Dichroism for 2<sup>nd</sup> and 3<sup>rd</sup> structure analysis of proteins as well as amino acid analyzer for determining the amino acid content of proteins are also available.

Biotechnology Research Center has the facilities for designing and expressing recombinant proteins and is equipped well from upstream to downstream processing of recombinant protein preparation (In analytical and semi preparative level).

**15. What kinds of difficulties do you face, in research and commercialization of medical biotechnology in your country?**

The main problem in research area which most of EMRO countries are faced is insufficient governmental investment on R&D as well as lack of transparent logics in establishing intellectual properties.

**16. Are there enough trained biotechnologists in the field of medical biotechnology in your country?**

It isn't enough but the outlook is promising.

Thank you Dr. Vaziri for your kind and useful cooperation.



## Quantitative PCR

PCR and its new versions have been accepted as widely used approaches in quantifying DNA samples because of its greater sensitivity in detecting low target quantities.

Quantitative PCR represents the amount of amplified DNA by using fluorescence molecules reporting fluorescence intensity. The approach can measure signal at the **end of the reaction** (called **endpoint semi-quantitative PCR**) or when the amplification procedure is going on (**real-time QPCR**).

**I. At the endpoint semi-quantitative PCR**, information will be gathered at the end of reaction, **usually after 30–40 cycles**, calculating the amount of template DNA present in PCR reaction. This method may have unreliable results due to limitations of PCR during last cycles (for example, low concentration of reagents as well as accumulation of inhibitors or inactivation of Taq DNA polymerase). These effects can cause differences in final detected fluorescence values irrespective to the initial template concentrations (Figure 1).

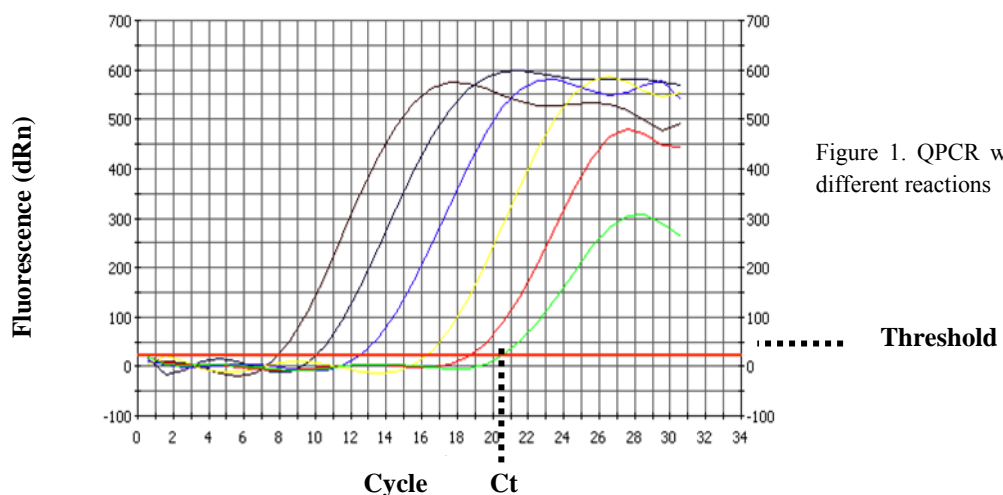


Figure 1. QPCR with different reactions

For purposes in which the researcher just tries to detect a target sequence, end-point QPCR measurements are generally desirable.

**II.** Quantification of initial template based on emitted signal during exponential phase of amplification will result in more sensitive and reliable method of real time QPCR. This approach does not have limitations of end point semi-quantitative PCR mentioned above.

Real-time QPCR needs a **fluorescent reporter molecule** (double-stranded DNA binding dye or a dye-labeled probe) for following the amplification reaction. Fluorescence intensity will increase proportionally at the end of each cycle due to the increase in PCR product concentration.

The background emitted fluorescence (called **baseline correction**) will be considered in drawing final plots of fluorescence vs. cycle number for each sample. A **threshold level** of fluorescence will be selected above the background but still **within the linear phase of amplification for all samples**.

The phrase 'Ct' or threshold cycle is referred to **the cycle at which the amplification plot crosses the threshold fluorescence level**. This Ct value can reflect directly the initial target DNA concentration within sample (Figure 1).

**Applications of real time PCR.** The applications of Real-time quantitative PCR are documented in quantification of gene expressions, expression profiling, single nucleotide polymorphism (SNP) analysis and allele discrimination, monitoring viral and bacterial loads as well as other pathogen-detection applications.

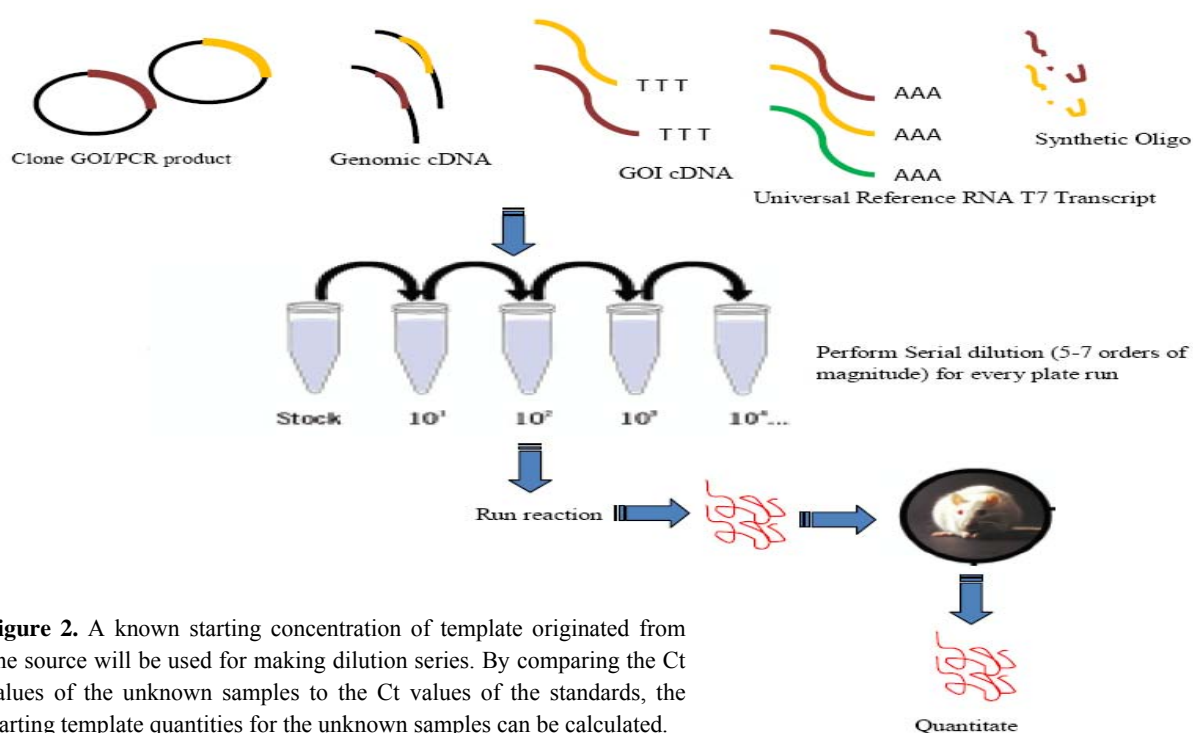
## Quantification methods

Two main quantification methods are available, standard curve and relative quantification with different applications.

### Standard Curve

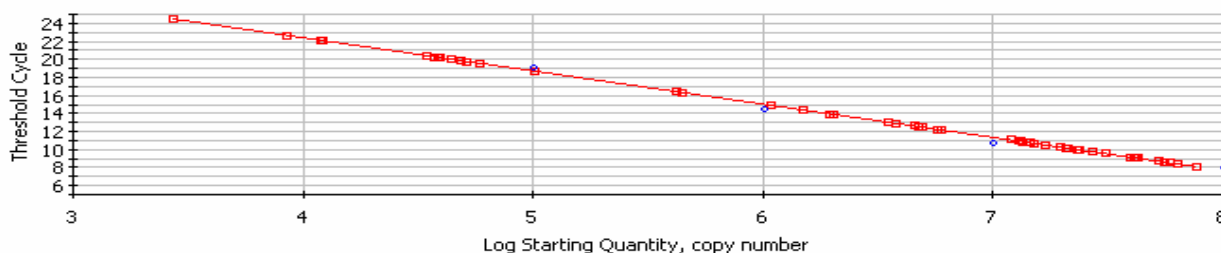
Using a standard curve is the most direct and reliable approach for quantitative approaches. The essential step is **preparing dilution series of known template concentrations**. This is known as “standard curve” or “absolute” quantification. This approach is widely used **to measure the exact concentration of template in the sample** (monitoring viral load in a sample).

Basic setup for standard curve quantification is described in Figure 2. Primers should be designed carefully to work efficiently with the standard molecules as well as the experimental source materials.



**Figure 2.** A known starting concentration of template originated from one source will be used for making dilution series. By comparing the Ct values of the unknown samples to the Ct values of the standards, the starting template quantities for the unknown samples can be calculated.

After amplification of the standard dilution series, the standard curve is drawn by plotting the log of the initial template copy number against the Ct obtained for each dilution. Careful aliquoting and accurate efficiency of the amplification will result to a linear regression line called the standard curve. Comparing the Ct values of the unknown samples to this standard curve reflects the quantity of initial copy numbers (Figure 3).



**Figure 3.** The log of the initial template quantity is plotted against the Ct values for the standard samples. By comparing the Ct values of the unknowns to this Standard Curve plot, the initial template quantities for the unknown samples can be determined.

## Chemical concept of QPCR

The fluorescent molecule used as the reporter in real-time PCR can be (1) a sequence-specific probe consist of a labeled oligonucleotide with a fluorescent dye plus a quencher or (2) a non-specific DNA binding dye such as SYBR Green I that fluoresces when bound to double-stranded DNA. Criteria that should be kept in mind in selecting the reporter for QPCR experiment are:

- The desired level of sensitivity and accuracy for analyzing obtained data
- The budget available for the project
- The skill and experience of the researcher in designing and optimizing QPCR reactions
- The number of DNA targets to be analyzed

## DNA Binding Dyes

DNA binding dyes such as **SYBR Green I** are cost effective and easy to use, especially for those researchers who are new to QPCR experiments. SYBR Green I represent low levels of fluorescence when it is free in solution, but its fluorescence intensity will increase when bound to double-stranded DNA. More binding sites will be available for dye when more double-stranded DNA is present which make an increase in emitted fluorescence. This property let the researcher to monitor the accumulation of PCR product in the reaction (Figure 4). To run the PCR reaction in the presence of the dye, designing a set of primers, optimization of the amplification efficiency and specificity are necessary.



**Figure 4.** SYBR Green I detection mechanism.

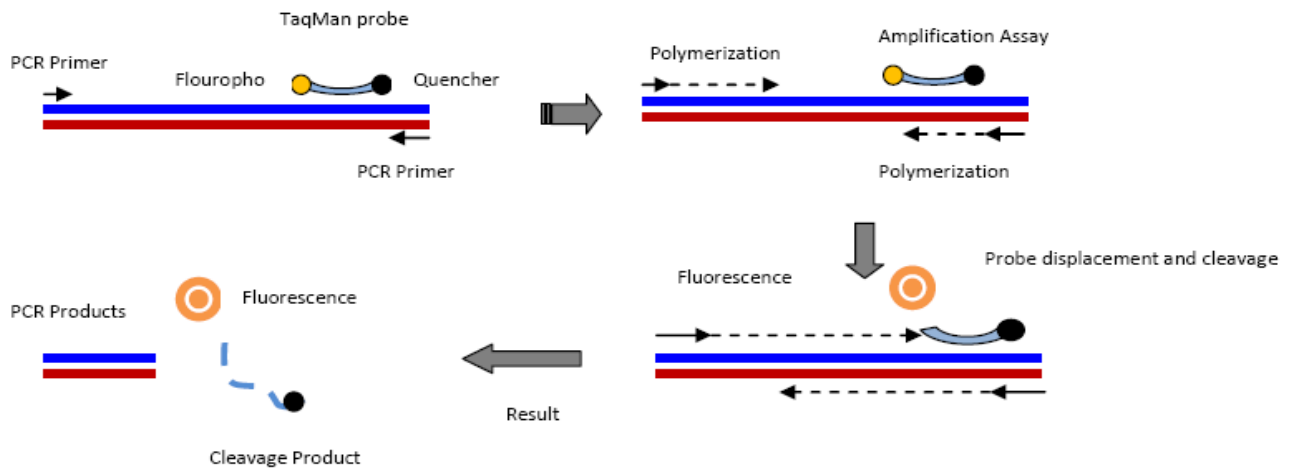
Non-specificity of SYBR Green I binding to any double stranded DNA is one of undesirable limitations of dye based assays. So, primers should be designed carefully to prevent non-specific bindings (e.g., primer dimer formation). In the other words, any non specific double stranded DNA formation can cause signal contamination resulting in artificially early Ct values, giving a wrong representation of the real target concentration.

The presence of more than one population of PCR products will be reflected as multiple thermal transitions in the fluorescence intensity. In this situation, the fluorescence versus temperature curve (known as the dissociation curve) is used to differentiate between specific and non-specific amplicons based on the  $T_m$  (melting temperature) of the reaction end-products.

## Probe-Based Chemistries

As compared to non-specific chemical dyes such as SYBR Green I, higher level of detection can be achieved by using an internal probe to detect the interested QPCR product. In the absence of specific target in the reaction, the fluorescent probe will not be hybridized, remains quenched, and does not fluoresce. When the probe hybridizes to the target sequence of interest, the reporter dye will not be quenched any more, and fluorescence will be emitted. The level of detected fluorescence is directly related to the amount of amplified target in each PCR cycle. A significant advantage of using specific probes is that multiple probes can be labeled with different reporter dyes and detection of more than one target in a single reaction can be applicable; a procedure which is called multiplex QPCR.





**Figure 5.** Probe based mechanism. These probes rely on the 5′–3′ nuclease activity of *Taq* DNA polymerase to cleave a dual-labeled probe during hybridization to the complementary target sequence.

## Different types of probes

### A) Linear Probes

Linear probes (i.e., hydrolysis or TaqMan probes) are the most widely used and published detection systems for QPCR assays. In addition to the PCR primers, a third oligonucleotide will be added to the reaction which is known as the probe. A fluorescent reporter dye is attached to the 5′ end of the probe and a quencher is attached to the 3′ end. TaqMan probes use a FRET (Fluorescence Resonance Energy Transfer) quenching mechanism where quenching can occur over a relatively long distance (100Å or more, depending on the fluorophore and quencher used).

The probe is designed to bind to one strand of the target sequence, downstream of one of the primers. As the polymerase extends that primer, it will reach to the 5′ end of the probe. When *Taq* DNA polymerase with 5′–3′ nuclease activity, reaches to the probe it degrades the 5′ end, releasing free reporter dye into the solution. After the separation of reporter dye and quencher, fluorescence can be detected from the reporter dye (Figure 5).

## B) Structured Probes

Structured probes contain stem-loop structures causing enhanced target specificity when compared to linear probes. This feature enables a higher level of discrimination between similar sequences and makes these chemistries suitable for SNP detection and allele discrimination applications. Molecular Beacons consist of a hairpin loop, where the central loop sequence is complementary to the target of interest and the stem arms are complementary to each other. One end (typically 5') of the stem is modified with a reporter fluorophore and the other end includes a quencher. The basis of Molecular Beacon probes is on ground-state or static quenching, which needs fluorophore and quencher in a very close distance for quenching occurrence. In the absence of the specific target, the Molecular Beacon's thermodynamic properties enhance the formation of the hairpin over mismatched binding. This property gives Molecular Beacons the increased mismatch discrimination that makes them well suited for applications such as SNP detection and allele discrimination (Figure 6).



**Figure 6.** Molecular Beacon chemistry mechanism.

**Reference:** Encyclopaedia of Medical Genomics and Proteomics, Edited by Fuchs J., Podda M., 2005, p 1117-1135.



# Biotech Center



**CENTRE FOR ARAB GENOMIC STUDIES**  
A Division of Sheikh Hamdan Award for Medical Sciences

## Introduction

The Arab World, due to its geography as well as its social customs, has gained a very unique position in terms of its genetic background. For instance, the wide-spread custom of relative marriages has led not only to a preponderance of genetic disorders in the region, but also to the presence of many genetic defects seen nowhere else in the world. A very large proportion of the population is affected by serious genetic defects. Added to this, the general lack of public awareness makes for a very grave state of affairs.

The diverse people across the Arab World present one of the greatest opportunities for the application of medical genetics. The study of constituent regional populations can form a new research resource from which scientists can bring fresh insights to the world genomics community.

In the Arab World, genetic diseases represent a major public health problem. Several factors contribute to the wide prevalence of genetic disorders in the region including the high rate of consanguinity, social trend to have more children until menopause, selective factors favoring inherited disease characters like thalassemia and glucose-6-phosphate dehydrogenase deficiency, and the lack of public awareness towards the early recognition and prevention of inherited disease.

The vision of **H.H. Sheikh Hamdan Bin Rashid Al Maktoum** is to alleviate human suffering from genetic diseases in the Arab World crystallized in the establishment of the Centre for Arab Genomic Studies (**CAGS**) to characterize and prevent genetic disorders and transfigure the future practice of health care in the region.

## History

The Centre was inaugurated on 25th June 2003 by H.E Hamad Abdul Rahman Al Midfaa, Minister of Health, and Chairman Board of Trustees of Sheikh Hamdan Bin Rashid Al Maktoum Award for Medical Sciences, at the Genetic Centre of Al Wasl Hospital. At present, offices of the Centre for Arab Genomic Studies are located within the premises of H.H. Sheikh Hamdan Bin Rashid Al Maktoum Award for Medical Sciences, Dubai, and UAE.



In 2004, the Centre for Arab Genomic Studies initiated a pilot project to construct the "Catalogue of Transmission Genetics in Arabs" (CTGA) database for genetic disorders in Arab populations. At present, the CTGA database, centrally maintained in Dubai, hosts entries for nearly 1240 Mendelian disorders and related genes and this number is increasing as researchers are joining the largest Arab scientific effort to define genetic disorders described in the region. The current version 6.56 of CTGA contains nearly 700 full-text records, including extensive data from the United Arab Emirates, Bahrain, and Oman. The CTGA database indicates that the populations it covers constitute a considerable resource for understanding single-gene disorders. The CTGA database development team include researchers working as database manager, data editor and curator.

## Objectives

Some of the priority objectives of the Centre for Arab Genomic Studies are:

- Educate the public and professionals alike on the important impact of genetic diseases in the Arab world and the methods and benefits of early genetic diagnosis
- Provide comprehensive genetic services by translating research achievements into well-integrated patient treatment programs
- Address the ethical, legal, and social issues that may arise with the implementation of such programs

## Scientific committees

CAGS includes two scientific committees: The Executive Board of CAGS and the Council of CAGS:

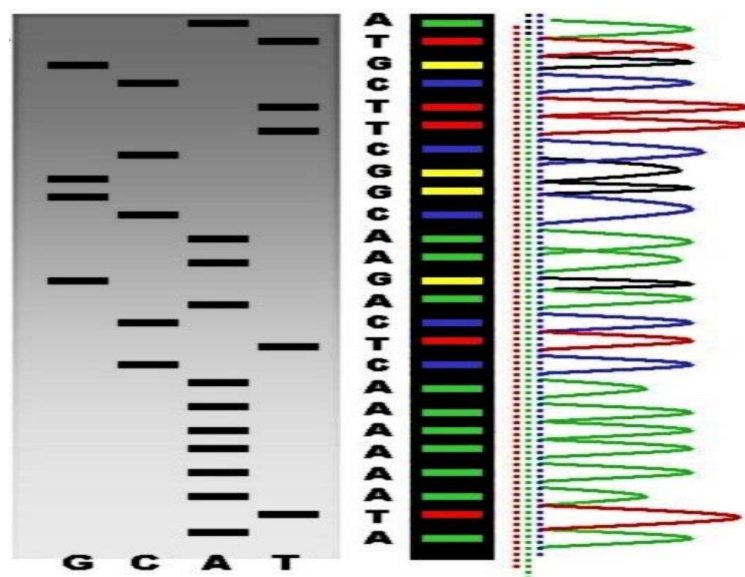
1. **The Executive Board of CAGS** is composed of a number of local scientists and represents the governing body and the legal trustee of all activities of the centre.
2. **The Council of CAGS** includes a number of regional scientists and it facilitates the exchange of information on genetic disorders occurring in Arab countries. Countries represented in the Council of CAGS currently include: Bahrain, Egypt, Jordan, Kuwait, Lebanon, Oman, Qatar, Saudi Arabia, Sudan, and Tunisia. In the future, CAGS aims to extend memberships to a larger group of scientists and include other Arab countries.

**Reference:** <http://www.cags.org.ae/index.html>



## *“Scientists decode first Arab genome”*

The first Arab human genome has been sequenced as part of a large project sequencing 100 genomes to map genetic variation in Arab people. Saudi Biosciences, in collaboration with the Beijing Genomics Institute Shenzhen, and the Denmark-based bioinformatics solution provider CLC bio announced the sequencing of Arab genome. Saeed Al-Turki, project coordinator at Saudi Biosciences, says that extensive studies have been carried out into the genetic differences in African, Asian and European populations and adding genetic attributes of the 400 million-strong Arabic population, who occupy many historical routes of human migration outside Africa, "will help to fill some gaps in the big picture".



Preliminary data shows interesting differences and raises the hope to narrow down causative variants for some common diseases like diabetes mellitus, which is a major health problem in the Middle East. It has been mentioned that the full Arab gene sequences will be added to the open access database GenBank along with other more specific international, regional and national databases.

Abdelaziz Sefiani, professor of medical genetics at the Morocco-based National Institute of Health of Rabat and founder of the Moroccan Human Mutation Database, says that the sequences will be a vital information source for Arab medical scientists and health professionals to develop cost-effective strategies for preventing, diagnosing and treating diseases. Finding links between human genes and certain diseases will help in developing genetic tests to identify people at risk and to tailor treatments to their genetic makeup.

But Princess Nisreen El-Hashemite, medical scientist and executive director of the Royal Academy of Science International Trust cautions that there is much work to be done in the legal and ethical spheres before genome sequencing technology becomes widespread. Publication of the data from the first genome is expected at the beginning of 2009, following completion of the data analysis.

### **Reference:**

<http://www.scidev.net>

<http://en.Wikipedia.org/wiki/file:Radioactive-fluorescent-seq.jpg>

## ***“UAE launches sight-saving initiative”***

The United Arab Emirates (UAE) for improving the treatment of blindness and visual impairment has launched a new universal programme for one million people in the UAE and developing countries. Last month Noor Dubai was launched and will fund new education programme for health workers, raise awareness and fund research.

It has estimated by WHO that up to 75 per cent of blindness cases and 90% of the blind reside in developing countries are avoidable. Anti-blindness education initiative will be a part of Noor Dubai's work to raise awareness and ensure that health professionals are equipped with the latest knowledge about technology and best practice. The organization will collaborate with the nonprofit organization ORBIS International on its Cyber-Sight telemedicine programme, which aims to connect eye doctors in developing countries with expert mentors from all over the world.

To set up educational programme and found guidelines and protocols for the supervising of eye diseases, ORBIS's Flying Eye Hospital, an airplane based hospital serving developing countries are associated. Funding for research is also on the agenda. Head of the Noor Dubai Medical Team and president of the Emirates Medical Association Ophthalmic Society, Manal Omran Taryam, says that Noor Dubai has received many proposals to fund research particularly for cataract, the leading cause of blindness in the world affecting 18 million people and making up 48% of blind cases. Tayaram says the budget for research funding has yet to be specified. He adds that Noor Dubai has been given an "open budget" by Sheikh Mohammed Bin Rashid Al Maktoum and the government of Dubai.



Morad Ahmed Morad, a professor of medicine at Tanta University, Egypt, says, "Noor Dubai must focus its anti-blindness research agenda on the evaluation of techniques that are cost-effective and easily accessible to developing countries, such as micronutrient supplementation, food fortification and other food-based programs". He adds that the organization should also evaluate new approaches to screening, diagnosis and salvation of eye care services, especially to underserved populations.

Iran has been received benefits from medical tourism and many individuals referred to medical centers in Tehran and Shiraz for their ophthalmic diseases every year. Now, It seems there is a competition between Iran and U.A.E medical centers in tourist attraction.

**Reference:** <http://www.scidev.net>



# Announcement



## **1<sup>st</sup> International Joint Conference on Materials Science, Nanotechnology and Biotechnology (MNB 09), Future Challenges**

**January 4-6<sup>th</sup>, 2009**

**National Research Centre (NRC), Cairo, Egypt**

### **Scope;**

Nowadays, materials science, nanotechnology and biotechnology are highly developing and challenging areas of research which are promoted every day. The conference will be hosted within the premises of NRC, one of the eminent multidisciplinary research centers in the Middle East, located in the heart of Cairo, Capital of Egypt.

### **Topics;**

#### **1. Advanced Materials:**

- Polymers
- Ceramic
- Biomaterial

#### **2. Nanotechnology:**

- Nano-Materials & Nano-Composites
- Optical & Electronic Materials

#### **3. Biotechnology:**

- Vaccine Challenge Technology
- Virology & Microbiology
- Cancer & Stem cell
- Animal Biotechnology
- Plant Biotechnology

**E-mail address:** [confunit@nrc.org.eg](mailto:confunit@nrc.org.eg)

#### **Reference:**

[http://ways.org/en/events/1st\\_international\\_joint\\_conference\\_on\\_materials\\_science\\_nanotechnology\\_and\\_biotechnology\\_mnb\\_09\\_future\\_challenges](http://ways.org/en/events/1st_international_joint_conference_on_materials_science_nanotechnology_and_biotechnology_mnb_09_future_challenges)





# Announcement



**International Centre for Genetic  
Engineering and Biotechnology  
(ICGEB)**

The Course on

**"The Analysis of Agricultural Products for the Presence of Genetically  
Modified Organisms"**

**10-12 May 2009, Tehran, Iran**



**National Institute of Genetic  
Engineering and Biotechnology  
(NIGEB)**

## **Theoretical course:**

- Introduction to GMOs and LMOs
- Detection of GMOs: DNA-based and Protein-based methods (Quantitative and Qualitative)
- Biosafety issues related to GMO contamination in agricultural products Practical

## **DNA-based detection methods for seed and food:**

- DNA extraction, Qualitative PCR and Real Time PCR

## **Protein-based detection methods for seed and food:**

- Lateral flow strips and ELISA

## **Eligibility criteria:**

Scientists involved in research related to the detection of genetically modified organisms and officers or designated experts working in the area of GMOs at an official level (governmental agencies, scientific institutions, private sectors, etc.). Preference will be given to applicants from developing countries.

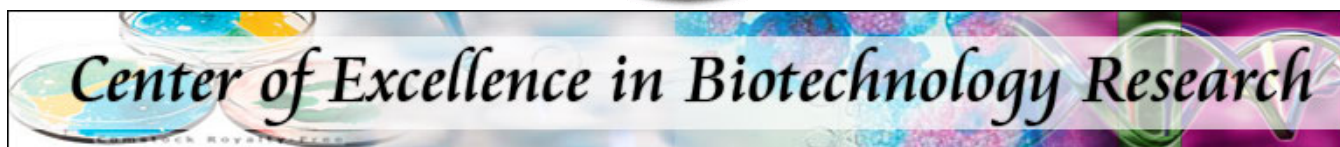
**Closing date for application:** 31 January of 2009

**Reference:** <http://www.nrcgeb.ac.ir>





# Announcement



## **“The First International Conference on Biotechnology”**

**21-23<sup>th</sup> Safar, 1430 (16-18<sup>th</sup> February, 2009)**

**Riyadh, Kingdom of Saudi Arabia**

**"Towards Knowledge Based Society"**

### **Main Objectives:**

- Applications of biotechnology in Medical Sciences
- Applications of Biotechnology in Agriculture
- Applications of Biotechnology in Environment and Industry
- Biotechnology as an Economical Resource

**Reference:** <http://www.cebr.ksu.edu.sa/>

**E-mail address:** [cebio@ksu.edu.sa](mailto:cebio@ksu.edu.sa)

## **Title: Protein kinase C, beta 1, also known as PRKCB1, is a human gene**

**Description:** Protein kinase C (PKC) is a family of serine- and threonine-specific protein kinases that can be activated by calcium and second messenger diacylglycerol. PKC family members phosphorylate a wide variety of protein targets and are known to be involved in diverse cellular signaling pathways. PKC family members also serve as major receptors for phorbol esters, a class of tumor promoters. Each member of the PKC family has a specific expression profile and is believed to play a distinct role in cells. The protein encoded by this gene is one of the PKC family members. This protein kinase has been reported to be involved in many different cellular functions, such as B cell activation, apoptosis induction, endothelial cell proliferation, and intestinal sugar absorption. Studies in mice also suggest that this kinase may also regulate neuronal functions and correlate fear-induced conflict behavior after stress. Alternatively spliced transcript variants encoding distinct isoforms have been reported. This gene could be associated with autism.

**Source:** <http://en.wikipedia.org/wiki/PRKCB1>

## **Title: Two Dimensional Gel electrophoresis**

**Description:** Images of two 2D electrophoresis gels overlaid and warped with Delta2D. First image is colored in orange, second one colored in blue. Corresponding spots overlap after warping. Common spots are colored black, orange spots are only present (or much stronger) on the first image, blue spots are only present (or much stronger) on the second image.

**Source:** <http://en.wikipedia.org/wiki>

## **Title: Real time quantitative PCR**

**Description:** Real time quantitative PCR using TaqMan probes is a multistep procedure. In the first step using intact TaqMan probes, reporter fluorescence is quenched due to Fluorescence Resonance Energy Transfer (FRET). (2) Probes and the complementary DNA strand are hybridized and reporter fluorescence is still quenched. (3) During PCR, the 5'-ends of the probe are degraded by the DNA Taq polymerase and the fluorescent reporter will be released.

**Source:** <http://en.wikipedia.org/wiki>

## **Title: DNA sequencing (Chain termination method)**

**Description:** While the chemical sequencing method of Maxam and Gilbert, and the plus-minus method of Sanger and Coulson were orders of magnitude faster than previous methods, the chain-terminator method developed by Sanger was even more efficient, and rapidly became the method of choice in DNA sequencing. The Maxam-Gilbert technique requires the use of highly toxic chemicals, and large amounts of radio labeled DNA, while the chain-terminator method uses fewer toxic chemicals and lower amounts of radioactivity. The key principle of the Sanger method is the use of dideoxynucleotides triphosphates (ddNTPs) as DNA chain terminators.

**Source:** <http://en.wikipedia.org/wiki>

