

# EMGEN Newsletter

Vol. 4, Issue 9, Jan 2013

## IN THIS ISSUE:

1. Article, P 2
2. Interview, P4
3. Training, P 7
4. Trends, P 11
5. Journal Alert, P 15
6. News, P 16
7. Web Link, P 17
8. Announcement, P 19
9. Cover pictures description, P 21

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

### Address:

Biotechnology building, #69, Pasteur Ave., Pasteur Institute of Iran  
Tehran, Iran, 13164

Tel: +98-21-66954324

Fax: +98-21-66465132

E-mail: [emhgbn@gmail.com](mailto:emhgbn@gmail.com), [secretariat@emhgbn.net](mailto:secretariat@emhgbn.net)

Website: [www.emhgbn.net](http://www.emhgbn.net)

**Prepared by:** Vida Sedighi

**Page design:** Vida Sedighi

**Helped by:** Mr. Golzarroshan and Ms. Hamidipour

**Assistant editor:** Mrs. Van Marle-Marschall, M.A

**Editor:** Dr. S. Sardari

## Frequency of Bcr-Abl Fusion Oncogene Splice Variants Associated with Chronic Myeloid Leukemia (CML)

The article Below, entitled "Frequency of Bcr-Abl Fusion Oncogene Splice Variants Associated with Chronic Myeloid Leukemia (CML)" was published in "Journal of Cancer Therapy", July 2011, vol. 2, pp 176-180. The study was carried out by Dr. Zafar Iqbal working at the Molecular Genetic Pathology Unit, Department of Pathology, College of Medicine and King Khalid University Hospital, King Saud University, Riyadh, Saudi Arabia as well as Hematology, Oncology and Pharmacogenetic Engineering Sciences (HOPES) Group, Health Sciences / Parasitology Research Laboratories, Department of Zoology, University of the Punjab, Lahore, Pakistan.



*Dr. Zafar Iqbal*

Chronic myeloid leukemia (CML) has been explained by the presence of Philadelphia (Ph) cytogenetically chromosome in 95-99% of CML patients. CML originates from the reciprocal translocation of chromosome 9 and 22 t (9; 22) (q34; q11), which gives rise to BCR-ABL fusion oncogene. This gene translates a chimeric protein, p210BCR-ABL explained by necessary activation of its tyrosine kinase activity. This constitutively active cytoplasmic tyrosine kinase enhances proliferation and viability of myeloid lineage cells and leads to development of CML. During the last decade, drugs like Imatinib, Dasatinib and Nilotinib and the advent of BCR-ABL inhibitors have revolutionized the treatment of CML. Drugs like Imatinib, Dasatinib and Nilotinib inhibit the tyrosine kinase activity of BCR-ABL protein leading to increased rates of hematological, cytogenetic and cytogenetic responses. Different types of BCR-ABL transcripts are associated with a different prognosis, treatment response that it making them useful and applicable in a therapeutic plan. Accordingly, this study was adjusted to calculate the frequency of BCR-ABL gene splice variants associated with CML. Tri-Zol method extracted RNA from peripheral blood and reverse-transcribed to cDNA were used as template in PCR reactions. A very sensitive nested RT-PCR was established to identity BCR-ABL splice variants in CML. The range of RT-PCR assay was of the order of  $10^{-6}$ . Two kinds of PCR products were discovered as 305bp and 234bp for b3a2 and b2a2 BCR-ABL splice variants. Both fusion transcripts frequencies obtained for b3a2 and b2a2 were 63.33% and 36.66% respectively. By generating 10-fold serial dilutions the sensitivity assay as to

nested PCR was found to be up to  $10^{-6}$  of cDNA for each sample.

Frequencies of BCR-ABL for evaluating the RT-PCR sensitivity for discovering these fusion transcripts have been reported. CML patients were found to be 21% and 62% for b2a2 and b3a2 respectively for frequencies of fusion transcripts in Iran. In 2005, De-Lemos and colleagues have reported statistically significant diversions in the expression levels of transcripts b2a2 and b3a2 at six months of imatinib exposure showing that b2a2 may have a molecular response better than b3a2. Rare variants like e1a2 have an inferior response to imatinib, as has been found by verma and colleagues in 2009. In 2010, Sharma has reported that 59% patients with the b2a2 kind gained complete cytogenetic response (CGR) as compared to 28% patients with b3a2 ( $p = 0.04$ ) while in 24 patients with minor or no CGR, 25% had b2a2 compared to 75% b3a2 b3a2 kind ( $p = 0.04$ ). However, expression of BCR-ABL/ABL% was higher in b3a2 patients compared to b2a2 ( $p = 0.120$ ). They have reported that pre-exposure characteristics like mean spleen size, mean hemoglobin, and mean platelet counts were not significantly different in the b3a2 vs. b2a2 transcripts groups, which supports our findings. These observations highlighted the need of more studies in different ethnic classes on the role of different BCR-ABL splice variants in biology and treatment response of the BCR-ABL positive leukemia patients, since acquired BCR-ABL point mutations, BCR-ABL amplification and other factors associated with imatinib resistance could not explain the reason of resistance related to drugs like Imatinib in all BCR-ABL positive patients. Concluding, BCR-ABL variants of splice frequencies can vary in different geographical regions due to interplay of natural genetic variations in different ethnic populations, diverse peripheral factors and life style. However, the data about the frequencies of BCR-ABL transcripts in CML can be of great significance as it can help to further understand the pathobiology of t(9;22)-positive leukemic cells. Most importantly, it can help in prognostic stratification, patient-tailored treatment and clinical management of drug resistance of CML in the modern era of molecularly targeted anti-cancer treatment.

## **Reference:**

Iqbal, Z.; Manzoor, F.; Iqbal, M.; Ali, S.; Sheikh, N.; Khan, M.; Khan, A.; Akhtar, T. *Frequency of Bcr-Abl Fusion Oncogene Splice Variants Associated with Chronic Myeloid Leukemia (CML)*, *J. Cancer Therapy*. **2011**, 176-180.



# Interview



In this issue, we present the following interesting interview with **Dr. Moien Kanaan** from Bethlehem University, head of the Biotechnology Division.

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

I am Moien Kanaan, an Affiliate Professor in Medical Genetics. I have obtained a B.Sc. In Nutritional Biochemistry from the University of Baghdad, Iraq, and an M.Sc. in Immunology from University of Arizona, Tucson, and a Ph.D. in Molecular Genetics from the Ohio State University, Columbus. After completing the North American education and training, I decided to go back, and I was Assistant Professor and Chairperson at Bethlehem University. From 2007 to the present I am Professor of Molecular genetics. I have a Hereditary Research Lab (details at: <http://hrl.bethlehem.edu> ). From 2000 to the present, I am Affiliate Professor at “Global Health Associate Scientist”, at the University of Toronto.



*Dr. Moien khanaan*

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

Medical and Population Genetics.

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

Because of my Ph.D. training, as well as the relevancy to the Palestinian population and the public health sector.

**4- Do you apply any biotechnology or genomics tools in your researches? If yes, please explain how and where?**

Yes and currently at the Hereditary Research Lab (HRL) at Bethlehem University

Tools are: A) Linkage analysis

B) Homozygosity mapping

C) Next generation sequencing

**5- What kinds of biotechnology facilities do you have in your laboratory?**

Genomic facility, PCR related work, Sequencing work (Sanger and NGS), Cell biology domains (functional studies) and Bioinformatics.

**6- Are there any biotechnology products that have been made in your country? (I.e. your native res-**



# Interview



**-researchers involved in the project)**

A sequencing array that tests for 247 hearing loss related genes and another array that tests for 20 breast cancer related genes.

**7- Are there any late stage biological products to be commercialized in your center? Could you please explain more?**

Not yet

**8- Are there significant biotechnology centers in your country?**

The HRL, the BECTEN biotechnology Center both at Bethlehem University. There are other research labs but not centers.

**9- Are there any academic training courses in Biotechnology in your country? If yes, please kindly describe at which level and how many students are trained annually?**

Master in Biotechnology, with a current enrollment of 50 students with an annual rate of 12-15 graduates.

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

No, I am not familiar. It was introduced to me two years ago in a conference in Dubai.

**12- Do you have any governmental support for biotechnology in your country? And at what level?**

Unfortunately no, but new initiatives are in the making.

**13- What kinds of difficulties do you face, in research and commercialization of medical biotechnology in your country and the region?**

Research funds and sustainability as well as private sector involvement and entrepreneurships.

**14- How many trained biotechnologists are there in the field of medical biotechnology in your country? Do you feel this number is enough? And what should be done if the answer is no.**

There are research labs that are utilizing biotechnology tools and I would say a total of a few hundreds. No, it is not. A new higher education initiative to address biotechnology adaptation and resource investment.

**15- Do you have any training courses or workshops in your research centre?**

Yes, but customized towards certain needs, such as fragment analysis and bioinformatics application.





# Interview



## **16- What is your idea about improvement of linkage between research and industry?**

It is mutual interest based approach towards product and service industry.

## **17- What is your opinion about the development of the biotechnology and genomics in your place?**

The Hereditary Research Lab (HRL) research activity and infrastructure constitute a major effort in building a national Genome Strategic Resource Laboratory for genome methodologies - large scale DNA sequencing, the detection of DNA variations (mutations, polymorphisms and chromosomal breakpoints), and computational genomics. This facility will provide genome-related practical know-how, as well as computing-intensive tools with regard to DNA sequence and variation analyses for the entire academic community of "The Palestinian Authority." Such strategic resource is essential for the future ability to benefit from the outcome of the world-wide Human Genome Projects (Hap map, 1000 Human Genome...etc).

It is expected to support new biotechnology enterprises in the areas of diagnostics, agriculture, combating genetic diseases, drug development and gene therapy.

The HRL reflects our conviction that the genetics of human populations present both the greatest challenge and the great opportunity for genetics in the future. We also believe that genetics of a people are most appropriately addressed by scientists who live in the same places as those people. Clearly this requires specialized training and sustainable transfer of technology.

The HRL offers practical and sustainable results for the Life Sciences Department at Bethlehem University. We have identified exactly the components of current genomics technology that can be directly transferred to Bethlehem University, which will be of practical use in medical and public health research in Palestine, and which will enable students at Bethlehem University to obtain up-to-date training in these disciplines. On the one hand and to research work in Palestine on the other.

## **18- Would you please tell us about the differences of biotechnology concepts and its applications between developed and developing countries? What should we do in this respect?**

The differences come from a market economy need that dictates the biotechnology direction in the developed countries while relevancy and outsourcing dictate biotechnology direction the developing countries.

***Thank you Dr. Moien Kanaan for sharing information and your opinion with us. Also we are grateful for your kind and useful cooperation.***



# Training



## Embryonic stem cells

Researcher eliminated a alone type of cell from a teratocarcinoma in 1964, a tumor now identified to be derived from a germ cell. These cells isolated from the teratocarcinoma replicated and raised in cell culture as a stem cell and are present identified as embryonic carcinoma (EC) cells. These genetic aberrations further emphasized the require to be able to culture pluripotent cells straightly from the inner cell mass. In 1981, employing mouse embryos by two department were independently first derived embryonic stem cells (ES cells). Martin Evans and Matthew Kaufman from the Department of Genetics, University of Cambridge, for the first time in July, released using a new method, the method of culturing mouse embryo in the womb of the license in cell number suggests, allows you to extract cells and ES of the fetus. In 1998, achieving success happened when researchers, led by James Thomson at the University of Wisconsin-Madison, first developed a technique to isolate and raise human embryonic stem cells in cell culture.

### Embryonic Stem cells (ES cells)

ES cells have been obtained from the inner cell mass of the blastocyst, an early-stage embryo. Human embryos should be made use of at the blastocyst stage 4– 5 days post fertilization, at which time they include 50–150 cells.

ES cells are distinguished by two distinctive properties:

- Their pluripotency
- Their ability to replicate indefinitely.

ES cells are defined as pluripotent with the ability to differentiate into all branches of the three initial germ layers: ectoderm, endoderm, and mesoderm. These include each of the more than 220 cell types in the body of an adult. In adults it was found that pluripotency distinguishes embryonic stem cells from adult stem cells; whereas embryonic stem cells can produce all kind of cells in the human of body, adult stem cells are multipotent and can manufacture a limited number of cell types. Body ES cells measure nearly 14 $\mu$ m while mouse ES cells are closer to 8 $\mu$ m.



# Training

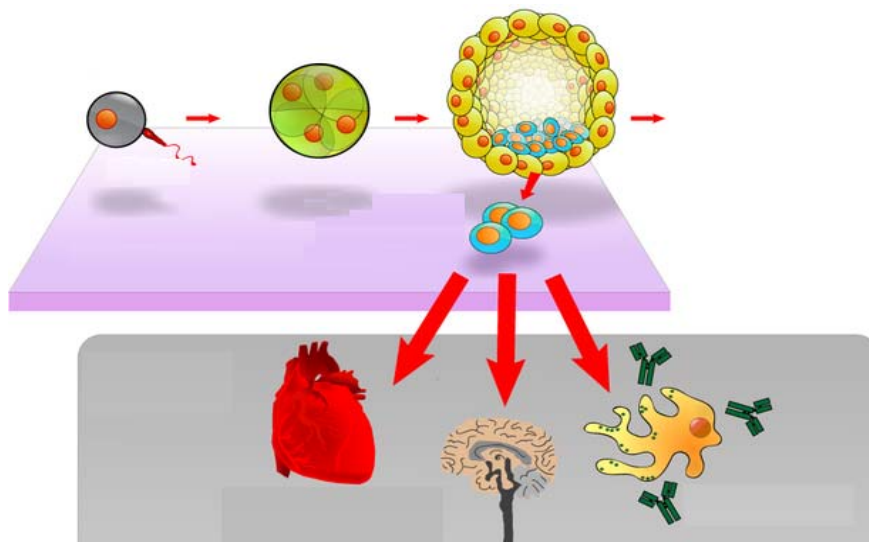


Several novel studies have been started on this issue. This involved either genetically tampering with the cells, or more recently extracting diseased cell lines known by prenatal genetic diagnosis (PGD).

Yury Verlinsky, a scholar of medicine who specialized in the field of embryo and cellular genetics (genetic cytology), established prenatal diagnosis assay techniques to detect genetic and chromosomal abnormality a month and a half earlier than standard amniocentesis. This technique is currently used by many pregnant females and prospective parents, particularly those couples with a history of genetic abnormalities or where the female is over the age of 35, when the rate of genetically-related disorders is higher.

In addition, by permitting parents to select an embryo without genetic disorders, they have the potential of preserving the lives of siblings that already had same disorders and illnesses utilizing cells from the disease free offspring.

Approximately, all studies to date have made use of mouse embryonic stem cells (mES) or human embryonic stem cells (hES). Both have the basic stem cell characteristics; though they require very diverse environments in order to maintain an undifferentiated stage. mES are developed on a layer of gelatin and require the Leukemia Inhibitory Factor (LIF).



*Techniques for Generating Embryonic Stem Cell Cultures*





# Training



Human ES (hES) cells are developed on a feeder layer of mouse embryonic fibroblasts (MEFs) and need the presence of basic Fibroblast Growth Factor (bFGF or FGF-2). The lack of optimal culture conditions or genetic manipulation will cause non-embryonic stem cells to rapidly differentiate. A human embryonic stem cell is also specified by the many transcription agents attendance and cell surface proteins.

## Culture of ES cells on feeder cells

### *1-First cultures on mouse-derived feeder cells*

Human ES cell lines were originally derived and propagated utilizing mouse fetal fibroblasts as feeder cells, similar to those employed in the derivation of mouse ES cell lines. The culture medium also involved fetal bovine serum (FBS). These animal-substance-including systems bear the subsequent danger of contamination with retroviruses and other pathogens, which could be transmitted to patients. It has also been demonstrated that the ES cells cultured under such conditions contain non-human sialoproteins with immunogenic effect on humans.

### *2-Cultures on human feeder cells*

Subsequently, human fetal muscle and skin as well as adult fallopian tube cells were utilized for the culture of available ES cell lines, and human serum was successfully employed in the propagation of one line. Skottman et al. derived novel ES cell lines using human foreskin fibroblast as feeder cells. After that they derived 25 ES cell lines on such feeder cells. Amit et al. used such cells for the maintenance of an existing ES cell line. Other human feeder cells used for derivation of novel ES cells are human placental fibroblasts, human endometrial cells, adult marrow stroma cells and ES cells-derived fibroblasts. In order to keep available lines, human feeder cells have been utilized by numerous groups.

Additionally, adult skin and muscle cell could support maintenance of ES cells. None of these culture systems were animal serum free when using FBS in the deployment of the feeder cells.

## Feeder-free culture of ES cells

### *1-Cultures on extracellular matrix*

The first feeder-free maintenance systems for accessible ES cells were cultured on Matrigel.



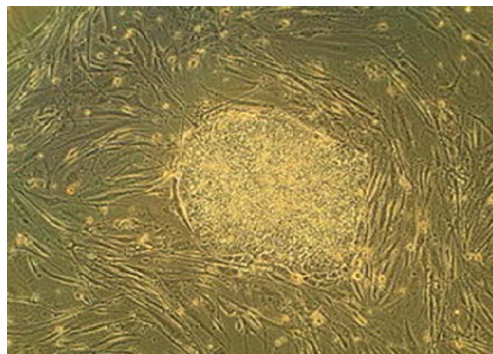
# Training



Matrigel is constructed from mouse material and consist of numerous extracellular matrix (ECM) components with containing several growth factors. A conditioned medium from fetal mouse fibroblasts permitted a non-differentiated growth of accessible ES cell lines on Matrigel. A non-distinctive growth up to 10 passages was investigated. For possible use in human cell transplantation, such ES cells could be extremely sub-optimal. The following developments were laminin and fibronectin as ECMs. Either conditioned medium from mouse fibroblasts, or combinations of growth factors (bFGF, TGF $\beta$ , activin A, Nodal, Noggin, LIF, and PDGF) were employed. The characteristic on the borders of the colonies can be seen in several of these reports.

## 2-Feeder-free derivation

A feeder-free derivation of ES cells has also proved possible. Mouse embryo fibroblast feeder free form ECM was used in the first successful derivation. In the first chemical study of the ECM Matrigel, derivation of ES cell lines is used to define the two, making this system ideal for the cell transplantation. Karyotype 47XXY is one of these lines, which is common in human embryos.



*Human embryonic stem cells in cell culture*

### **References:**

- 1-[http://en.wikipedia.org/wiki/Embryonic\\_stem\\_cell](http://en.wikipedia.org/wiki/Embryonic_stem_cell)
- 2-<http://www.news-medical.net/health/What-are-Embryonic-Stem-Cells.aspx>
- 3- Skottman, H.; Dilber, M. S.; Hovatta, O. *The derivation of clinical-grade human embryonic stem cell lines*, *J. FEBS Letters*. **2006**, 2875–2878.



## Reverse genetics

Reverse genetics is a technique to investigate the function of a gene by analyzing the phenotypic impacts of specific gene sequences obtained by DNA sequencing. This investigation process ensues in the opposite opposite to so-called forward genetic screens of classical genetics. In fact, reverse genetics tries to find what phenotypes arise as the result of specific genes.

Automated DNA sequencing generates a large amount of genomic sequence data of fair quality. Many genetic sequences, as has been discovered, do not easily provide biological information. The purpose of reverse genetics is to connect a given genetic sequence with certain effects.

### Techniques used in reverse genetics :

#### *1-Directed deletions and point mutations:*

Site-directed mutagenesis would be defined as a complex procedure, viz. any change in the gene promoter or regulatory regions can cause subtle changes in codon open reading frame to the amino residues of protein function.

Frequently, the technique can be used to create null alleles when a gene is not functional. For instance, deleting a gene by gene targeting (gene knockout) as can be done in some organisms, such as yeast, mouse and moss.

The yeast model systems have been directed to remove all non-essential genes in the yeast genome. The plant model systems have large libraries of mutant genes of affected structures. In gene knock-in, the endogenous exon is replaced by a change sequence of interest. In some cases conditional alleles can be used when the gene has normal performance until the conditional allele is activated. It may require 'knocking in' recombinase sites (such as lox or frt sites) that will cause an elimination at the gene of interest when a particular recombinase (such as CRE, FLP) is induced. Cre or Flp can be induced with chemically, or with heat shock, or be restricted to a particular subset of tissues.

Another method that can be utilized is TILLING. The combination of a standard and efficient muta

# Trends



-genesis with a chemical mutagen such as ethyl methanesulfonate (EMS) with DNA sensitive screening is a technique to detect single base mutations (also called point mutations) in target gene.

## *2-Gene silencing*

Gene silencing involves double stranded RNA known as RNA interference (RNAi). RNAi creates a particular knockout effect without actually mutating the DNA of interest.

In *C. elegans*, RNAi has been used for systematically interfering with the expression of most genes in the genome. RNAi acts by directing cellular systems to reduce purpose messenger RNA (mRNA).

Though RNA interference relies on cellular parts for efficacy (e.g. the Dicer proteins, the RISC complex), an easy replacement for gene knockdown is Morpholino antisense oligos. Morpholinos bind cellular proteins and mRNA activity without the need to accelerate block access to target mRNA is reduction. Morpholinos are efficient in domain systems for cell-free translation during *in vivo* test tube studies in large animal models.

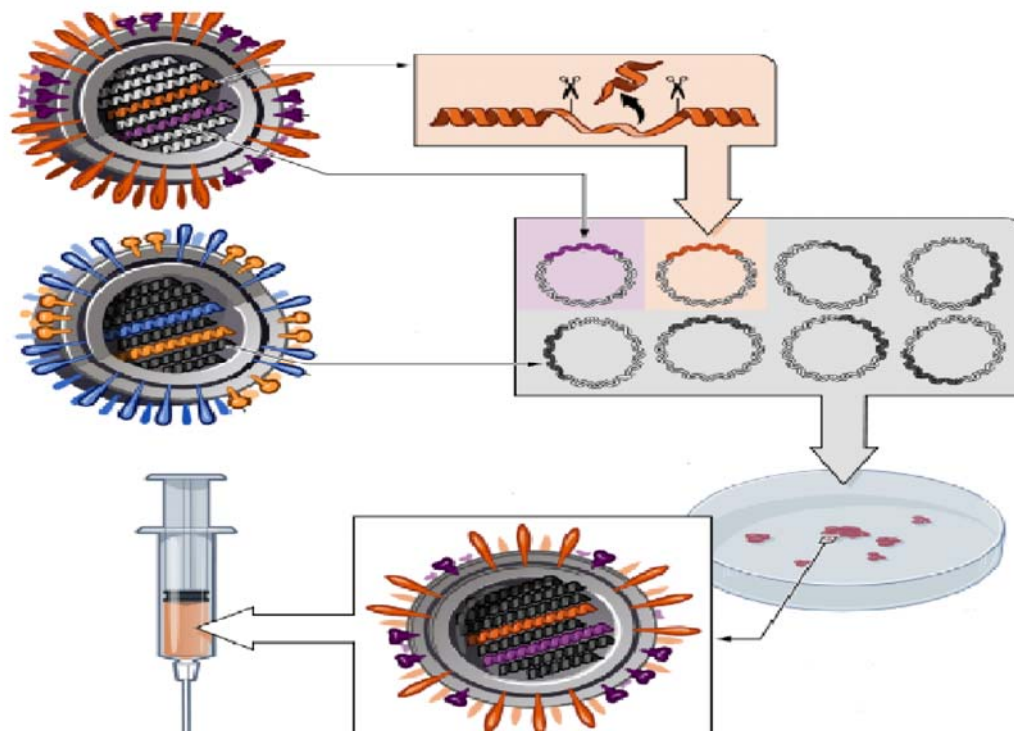
## *3- Interference using transgenes*

It could be defined as a molecular genetic method that certain transgenic organisms over-express a specific normal gene. The resulting phenotype may show the normal attributes of the gene.

Alternatively, it would be obvious that over-expressing mutant forms of a gene could interfere with the normal (wild type) genes function. For instance, over-expression of a mutant gene may have an impact on high levels of a non-functional protein so that it can end up with a dominant negative interaction between the wild type proteins.

Other mutant forms can occur in a protein that is unusual in its regulation and constitutively active ('on' all the time). This may be due to the elimination of a regulatory domain or mutation of specific amino residues that is reversible (methylation, phosphorylation or ubiquitination). Both changes are very important for modulating protein function and often leads to informative phenotypes.





*Avian Flu vaccine development by Reverse Genetics techniques*

## Reverse chemical genetics approach to identify druggable gene products in Alzheimer's disease

In this study, reverse chemical genetic screening was employed to identify small molecule inhibiting BACE1-mediated cleavage of APP to ultimately investigate a putative target protein with desirable inhibitory effect. In order to identify inhibitor agents with a novel mechanism, a cell-based method and untouched neuronal cells were developed based on antibody-mediated selective capture of the BACE1-derived secreted APP ectodomain (sAPP $\beta$ ) fused to a secreted alkaline phosphatase (SEAP) reporter.

By utilizing mentioned cell system for screening in small molecule libraries, scientists identified small molecules that can inhibit BACE1-mediated cleavage of APP without directly interfering with BACE1 activity. Findings showed that a compound (termed C2) can reduce A $\beta$  levels in originally cultured neurons; also a mouse model of AD showed that it could be defined as applicable approach in the field of Alzheimer's biomedical investigations.



## Harnessing arenavirus reverse genetics for the development of novel strategies to combat human pathogenic arenaviruses

A wide range of *in vitro* and *in vivo* investigations have demonstrated the prophylactic and therapeutic value of the nucleoside analogue ribavirin (Rib) against many arenaviruses. Results showed that the gear can be both morbidity and mortality associated with infections in humans LAS, a reduction in the MAC infection and JUNV. Two identified limitations of Rib therapy based method could be defined as the need of intravenous administration for optimal efficacy and their significant side effects including anemia and congenital disorders.

Several of IMP dehydrogenase inhibitors as S-adenosylhomocysteine (SAH) hydrolase, a variety of sulfated polysaccharides, compounds phenothiazines, brassinosteroids and myristic acid have been reported against the arenaviral. However, these compounds showed only modest and rather non-particular effects associated with significant toxicity. There is an urgent need for investigating novel effective anti-arenaviral drugs.

Accordingly, a recent high-throughput screening (HTS) based on virusinduced cytopathic effect (CPE)-based assay was used to identify a potent small molecule inhibitor for TACV and many other NW arenaviruses.

### **References:**

1-[http://en.wikipedia.org/wiki/Reverse\\_genetics](http://en.wikipedia.org/wiki/Reverse_genetics)

2-Kim, T. W. *Reverse chemical genetics approach to identify druggable gene products in Alzheimer's disease*, *J. Alzheimer's and Dementia*. **2010**, S93–S94.

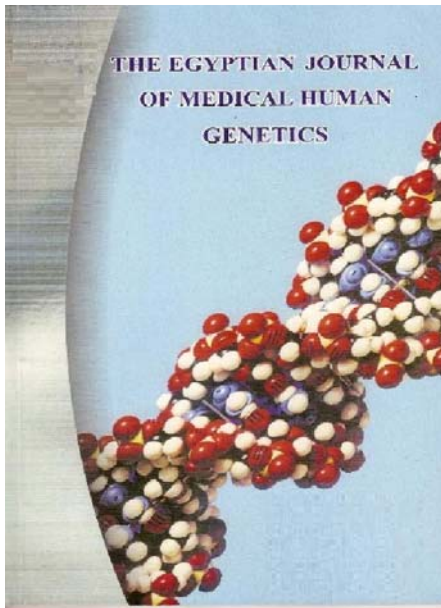
3-Emonet, S. E.; Urata, S.; Torre, J. C. *Arenavirus reverse genetics: New approaches for the investigation of arenavirus biology and development of antiviral strategies*, *J. Virology*. **2011**, 416–425.

# Journal Alert



## Egyptian Journal of Medical Human Genetics:

The Egyptian Journal of Medical Human Genetics publishes papers reporting original research in the field of human genetics and medicine. The Journal is a publication of the Society of Human Genetics, Medical Genetics Center, Ain Shams University, Egypt.



The fields included in the journal are:

- Biochemistry
- Molecular genetic and structural biological studies of enzymes
- Cell biology
- Protein deficiencies
- Fundamental investigations of the pathogenesis of inherited diseases

In addition to basic research, feasible progress in biochemical and molecular detection of human diseases will be considered a valuable contribution. The journal is now indexed by Chemical Abstracts Service, Pro Quest Star Here, African Journals On Line (AJOL), EBSCO Publishing, WHO Index Medicus, Deutsche Zentralbibliothek für Medizin, Index Copernicus Journal Information, Bibliotheca Alexandrina.

You can find all information via these titles:

Conflict of interest, Patient details, Submission, Introduction, Subjects and methods, Theory/calculation, Results, Discussion, Conclusions, Appendices.

The Editor-in-Chief is Prof. Dr. Rabah Mohamed Shawky and his email is [Shawkyrabah@yahoo.com](mailto:Shawkyrabah@yahoo.com) and [Rasha217@hotmail.com](mailto:Rasha217@hotmail.com). The Associate Editor is Prof. Mohamed S. El-Kholy and his email is [Elkholym@link.net](mailto:Elkholym@link.net). As to questions about details arising after the article is accepted, especially those relating to proofs, they will be dealt with by the publisher.

### **Reference:**

<http://www.ejmhg.eg.net/index.html>



## Design and characterization of sulfobetaine

The sulfobetaine methacrylate (SBMA) monomer was synthesized by the reaction of dimethylamino ethyl methacrylate and propane sultone.

These compounds have been used for blood contacting biomedical device applications. Free radical polymerization produced the terpolymer in 50 ml of solvent. The solvent was purged with argon for a minimum of 2 h to remove oxygen, then 10 g of the desired monomer mixture was added to the reaction vessel and purged for an additional 1.5 h. The monomers used in the reaction were n-hexyl methacrylate (HMA), methyl methacrylate (MMA), and SBMA. The temperature was increased to 55–60 °C and the desired amount of 2,2-azobisisobutyronitrile (AIBN), a free radical initiator, was added.

### Biological characterization:

The biological properties of terpolymer compounds were probed by interactions with blood components:

- fibrinogen – the blood protein which crosslinks to form fibrin clots – was used as our model protein in protein adsorption assays;
- HUVECs were used to assess the adhesion and growth capacity of adherent cells to these materials;
- Platelets were used to assess the thrombogenic nature of the surface.

Stuart L. Cooper et al. have explained these data as follows: "we see a near-confluent monolayer of endothelial cells on the Permanox positive control and on the Z0 materials (panels A and B). The Z5 materials have a large number of adherent HUVECs; however, these cells are not highly spread, indicating that they may have increased difficulty inhabiting the Z5 interface (panel C). The Z15 surface has large areas unoccupied by cells, similar to what is observed on the P15 negative control (panels D and E). In these experiments HUVECs were incubated with on Permanox and Z15 (the test material which contains the highest concentration of charged sites) for 3 h.

### Reference:

Heath, D. E.; Cooper, S. L.. *Design and characterization of sulfobetaine-containing terpolymer biomaterials*, *J.Acta Biomaterialia* . **2012**, 2899–2910.



# Web Link



## Genetic Health

In this issue we would like to introduce the Genetic Health web site (<http://www.genetichealth.com>).

In 1999, Scott Cole electronic health established Genetic Health, Inc. (GHI).

A screenshot of the Genetic Health website homepage. The header features a yellow and blue logo on the left and the text 'Genetic Health' in a large, blue, serif font. To the right of the header is a button labeled 'About Us'. Below the header is a navigation menu with a blue background and white text, listing 'Tools', 'Medical Glossary', and 'Genetics 101'. Under 'Genetics 101', there is a list of topics: 'Overview of Genetics', 'Inheritance Patterns', 'DNA Mutations', 'Changing Your Risk', 'Genetics and the Future', 'Personalized Medicine', 'Ashkenazi Jewish Genetics', and 'Inherited/Sporadic Cancer'. On the right side of the page is a large photograph of two men, one older and one younger, both smiling and embracing each other.

This site is helping to learn the latest about genetics and health and act to take control of health.

Genetic Health web site help by **Medical Glossary** in the tools and in this site exploring disease section such as Alzheimer's, Breast Cancer, Colon Cancer, Diabetes, Heart Disease, Hemochromatosis, Ovarian Cancer and associated this diseases with genetic or genes could be cause these diseases? If answer this question is yes, this site helping that is genetic testing available.



# Web Link



**Overview** of the tools and database that could be accessed through genome and genes. If you have been needed more information about “Genetics and the Future of Medicine” click on the link.

**Ethical issue part** of the web site is concerns to genetic discrimination and genetic information and health assurance.

**Research Participation** parameter on the left of the page summarizes the list of available tools to look for types of clinical trials and their listing.

**Frequently Asked Questions (FAQ)** part of the web site aims to answer questions on subjects such as: Why is genetics important?, What kind of information and tools does GH offer?, Who should use GH's web site?, Why does GH only focus on certain diseases?, Is the GH's site a substitute for the advice of my doctor?, Does GH eliminate the need to see a genetic counselor?

The web sit also provides some other useful information such as:

- 1– Genetics counseling
- 2– Obtaining Medical Records
- 3– Help for adoptions
- 4– Find a support group

If you have more information, you can search ihis site.

**Reference:**

<http://www.genetichealth.com>





# Announcement



<http://www.libpubmedia.co.uk/Conferences/RNAi2013/RNAiHome.htm>



8th International Conference and Exhibition

 **RNAi2013**

 19-21 March 2013  
St Hilda's College  
Oxford, UK

The banner features a photograph of the dome of St Hilda's College on the left. The text is centered and right-aligned. The RNAi2013 logo consists of a green circle with a white 'L' shape inside. A small image of a purple hibiscus flower is placed to the left of the date and location information.

<http://www.icddt.com/>



5<sup>th</sup> INTERNATIONAL CONFERENCE  
ON DRUG DISCOVERY & THERAPY

February 18<sup>th</sup> - 21<sup>st</sup>, 2013, Dubai, UAE

The banner has an orange background. On the left is a logo for the 5th International Conference on Drug Discovery & Therapy, featuring a blue globe and orange pills. On the right is a photograph of the Burj Khalifa and Burj Dubai in Dubai, UAE.

<http://www.iccma.net/>

**International Conference on Computer Medical Applications  
ICCMA' 2013 , January 20-22  
Sousse, Tunisia**



# Announcement



<http://www.icfbi.org/>

The banner for ICFBI 2013 features a blue background with a grid of colored squares (pink, blue, orange, green) on the left. The text 'ICFBI 2013' is prominently displayed in white. Below it, the full name of the conference, dates, and location are listed. Logos for JOIG and SCIEI are also present on the right side.

**ICFBI 2013**  
2013 International Conference on Functional Biomedical Imaging  
February 23-24, 2013  
Ho Chi Minh City, Vietnam

JOIG  
Journal of Image and Graphics

SCIEI  
www.sciei.org

<http://www.icbbb.org/>

The banner for ICBBB 2013 has a green background with a blurred image of white flowers. The text 'ICBBB 2013' is in large white letters. The location and dates are also included. The logo for IJBBB is on the right.

**ICBBB 2013**  
Rome, Italy February 24-25, 2013  
2013 3rd International Conference on Bioscience, Biochemistry and Bioinformatics

IJBBB  
ISSN 2010-3030

[http://www.smi-online.co.uk/pharmaceuticals/uk/  
pharmaceutical-microbiology](http://www.smi-online.co.uk/pharmaceuticals/uk/pharmaceutical-microbiology)

## Pharmaceutical Microbiology

30th January to 31st January 2013, London, United Kingdom



# Cover Picture



## **Title: Glioblastoma multiforme**

Glioblastoma multiforme (GBM) is an aggressively malignant primary brain tumor, which is most prevalent in human beings. It contains glial cells and accounts for 52% of all brain tumor cases and 20 percent of all lethal cancers. Our explanation is based on the classification of WHO for tumors of the central nervous system. The standard name for this brain tumor is "glioblastoma". It presents two variants: giant cell glioblastoma and gliosarcoma. Glioblastoma is also an important brain tumor in canines and as such used as an efficient model for developing clinical studies as well as procedures for treatment in the human body. Treatment may include chemotherapy, radiotherapy, radiosurgery, corticosteroids, therapy, antiangiogenic therapy, surgical procedures, and at an experimental stage gene transfer.

**Reference:** <http://en.wikipedia.org/wiki/Glioblastoma>

## **Title: Immunohistochemistry**

Immunohistochemistry (IHC) is a technique that detecting antigens such as proteins in cells of a tissues, This process is based on the principle of antibodies which binding specifically to antigens in tissues. IHC is a diagnosis tool for detect of abnormal cells such as cells in cancerous tumors. This technique is used in basic research as well that it helps to understand the localization and distribution of biomarkers.

**Reference:** <http://en.wikipedia.org/wiki/Immunohistochemistry>

## **Title: Alternative splicing**

Replace splicing is a process by which the exons of the RNA manufactured by transcription of the gene (the gene transcript or pre-mRNA gene) in multiple ways during RNA splicing, is interrupted. The various resulting mRNAs may be translated into other protein isoforms; thus, a single gene may code for multiple proteins. Replace splicing happens as a natural hazard in eukaryotes, where it greatly enhances the diversity of proteins which can be coded by the genome; in humans, ~95% of multiexonic genes are alternatively spliced. Multiple modes of Replace splicing have been observed to be the most popular exon jumping. If this mode occurs, a particular exon may be included in mRNAs under certain conditions or in particular tissues, and deleted from the mRNA in others.

**Reference:** [http://en.wikipedia.org/wiki/Alternative\\_splicing](http://en.wikipedia.org/wiki/Alternative_splicing)

