

# EMHGBN Newsletter

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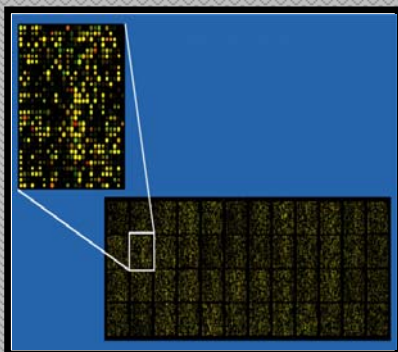
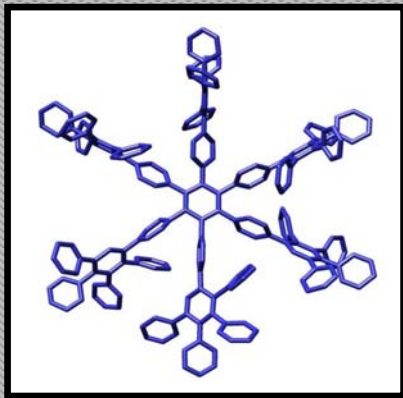
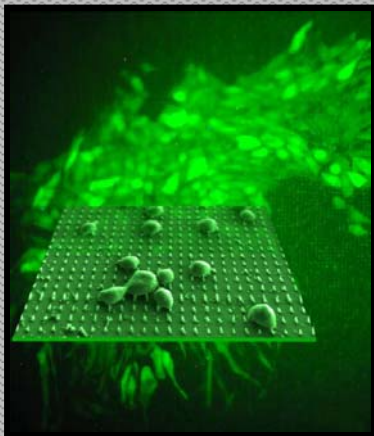
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Eastern Mediterranean Health Genomics and Biotechnology Network (EMHGBN) was created in 2004 with collaboration of representatives of selected centre of excellence in (health related) molecular biology, biotechnology & genomics in the Eastern Mediterranean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

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# Articles

## **Antiviral activity evaluation of *Aloe vera* from South-West of Iran against herpes simplex virus type 2: An *in vitro* study**

**By: Keivan Zandi**

*An article entitled “Antiviral activity of Aloe vera against herpes simplex virus type 2: An in vitro study” published in African Journal of Biotechnology Vol. 6 (15), pp. 1770-1773, 6 August 2007 deals with antiviral activity of Aloe vera extracts against HSV-2. Herpes simplex virus type 2 (HSV-2) is an enveloped virus which causes genital herpes and some other important complications. Finding new and natural anti-HSV-2 drugs has been a subject of interest for scientists because of severe side effects and the development of some resistant mutants of this virus. There are some publications about antiviral properties of different kinds of plant extracts such as Aloe vera, especially investigation about the antiviral activity of its anthraquinones. Regarding several environmental factors effecting chemical and biological composition of Aloe vera, it is tried to evaluate Anti HSV-2 activity of this plant grown in the south west of Iran.*

### **Materials and Methods**

**Cell line and virus and cytotoxicity test:** Vero cells were used for HSV-2 replication and propagation. Herpes simplex virus type 2 was isolated from clinical sample. The cytotoxicity of extract was determined by culturing of Vero cells for 72 hours in the presence of increasing amounts of extract. Then viable cells were determined by the trypan blue exclusion test. The results were plotted at dose response curve, and by using STATA statistical software, the 50% cell growth inhibitory concentration (CC<sub>50</sub>) was obtained.

**Antiviral activity assay:** A 24-well plastic plates of confluent Vero cells was prepared and culture medium was removed from each well. 0.1 ml of virus suspension containing 10000 TCID<sub>50</sub> and 0.1 ml of DMEM containing 2% FBS were mixed in each well of 24-well plates and appropriate concentrations of the extract from minimal to maximal non-cytotoxic concentration were added to each well based on serial dilution preparation. For the virus control 0.1 ml of virus suspension and 0.1 ml of culture medium without extract were used. For the cell control 0.1 ml of culture medium with maximal non cytotoxic concentration of extract were added. Also for evaluation of probable antiviral effect of 10% glycerine solution 0.1 ml of virus suspension and 0.1 ml of sterile 10% glycerine solution without extract were used. The plates were incubated at 37°C in a humidified CO<sub>2</sub> atmosphere (5% CO<sub>2</sub>) and were investigated everyday for CPE presentation until 5 day post infection. For testing the probable post attachment antiviral effect of the extract, same protocol which mentioned above was done but the adding of the extract was two hours post inoculation of cells with virus. The degree of inhibition was expressed as percent yield of virus control (% virus control = CPE experimental group/ CPE virus control 100). The concentration of extract which reduced CPE 50% with respect to virus control was estimated from graphic plots defined as 50% inhibited concentration (IC<sub>50</sub>) expressed in microgram per millilitre by using STATA modelling software. The selectivity index (SI) was measured from the ratio of CC<sub>50</sub>/IC<sub>50</sub>





# Articles

**Preparation of *Aloe vera* extract:** *Aloe vera* was collected from the pilot farm of the Jihad Keshavarzi Research Centre Bushehr (South west of Iran). The extracted fresh gel of *Aloe vera* was dissolved in 10% glycerine solution (20 minutes and 105 °C) and clarified by filtration using Whatman filter paper and Then was sterilized by autoclave.

## Results and Discussion

The cytotoxicity of *Aloe vera* gel crude extract on Vero cells was determined by calculation of  $CC_{50}$  which was 3238  $\mu\text{g/ml}$ . Antiviral activity: Based on resulted data we understood that the  $IC_{50}$  of this extract was calculated 428  $\mu\text{g/ml}$ . Regarding the resulting  $IC_{50}$  and  $CC_{50}$  from extract, the SI values was 7.56 for *Aloe vera* gel, hot glycerine extract. In post attachment stages of research the  $IC_{50}$  value and SI for filtered extract were calculated 536  $\mu\text{g/ml}$  and 6.04. This is the first study about the anti HSV-2 activity of hot glycerine extract of *Aloe vera* which were grown in Bushehr (South-West of Iran) . We have prepared hot glycerine extract of *Aloe vera*, because the glycerine extract enriched, for anthraquinones present in the plants. For the sterilization of the extract we have used autoclave, and we have found that the autoclaved extract showed the acceptable  $IC_{50}$  and based on SI values of this extract, it could be a good choice for anti- HSV-2 natural compound.



Dr. Keivan Zandi, Persian Gulf Health Research Centre, Bushehr University of Medical Sciences, Bushehr, Iran.





# Articles

## **Outcome of chromosomally abnormal pregnancies in Lebanon: obstetricians' roles during and after prenatal diagnosis**

**By: Laila F. Zahed**

*The study was performed at the American University of Beirut Medical Centre in Lebanon in collaboration with the Centre for Genetic Medicine and Medical Humanities and Bioethics at Northwestern University in Chicago, in order to better understand the experience of obstetricians in Lebanon when disclosing abnormal amniocentesis results .this paper was entitled “Outcome of chromosomally abnormal pregnancies in Lebanon: obstetricians' roles during and after prenatal diagnosis “and was published in Prenatal Diagnosis, vol. 27, no. 6, pp. 525–534, 2007,it was contributed by Lama T. Eldahdah, Kelly E. Ormond, Anwar H. Nassar, Tayma Khalil, Laila F. Zahed .*

Structured interviews were conducted with 38 obstetricians identified as caregivers from the Cytogenetic laboratory database of patients with abnormal amniocentesis karyotype results between 1999 and 2005. Obstetricians were primarily male and Christian. They reported doing most pre-amniocentesis counselling, including discussion of risk for common autosomal aneuploidies (95%), and procedure-related risk (95%). Eighty per cent of their patients at risk for aneuploidy elected to undergo amniocentesis. The study population reported on 143 abnormal test results (124 autosomal abnormalities). When disclosing results, obstetricians reportedly discussed primarily physical and cognitive features of the diagnosis. They varied in levels of directiveness and comfort in providing information. The records showed that 59% of pregnancies with sex chromosome abnormalities were terminated compared to 90% of those with autosomal aneuploidies; various reasons were proposed by obstetricians.

This study is among the few to assess prenatal diagnosis practices in the Middle East, with a focus on the role of the obstetrician. Given the influence of culture and social norms on prenatal decision making, it remains important to understand the various impacts on clinical practice in many nations.



**Dr. Laila F. Zahed**





# Training

## Toward a new era in sequencing

**Abstract.** Sequencing is a robust tool that helps scientists in gaining new understanding in many areas of medicine and biology. The electrophoresis-based Sanger method is at present the most popular sequencing technology and was the cornerstone of the human genome project. These days, this standard method is very close to attain its limits.

### Sequencing technologies of the next generation

Thanks to sequencing we now discern much more about the molecular principles of diseases. New discoveries about drug resistance have been reached via comparative sequencing of drug resistant genomes of pathogenic microorganisms and their drug sensitive equivalents.

The electrophoresis-based Sanger method has been gradually improved over the past 10 years. During this period sequencing expenses have fallen by about 90% while, at the same time, the output of a modern automated sequencer has increased 10-fold.

If sequencing is ever to develop into a component of personalized diagnosis and preventive medicine – and the potential is surely there – the costs must be decreased still further. The international planning goal is 1,000 dollars for an entire human genome.

Pharmaceutical sector also benefit from new sequencing technique, for instance in research on drug resistance and the pathogenicity of bacteria, for determining human DNA variations, establishing the onset of drug resistance in HIV or HCV, creating tumour profiles as a lead to cancer treatments or for distinguishing the modes of action of antibiotics.

### *Microelectrophoretic methods*

Microelectrophoretic techniques are based on existing technologies of capillary electrophoresis used in Sanger sequencing. One benefit is a smaller electrophoresis platform – with subsequent savings on reagent expenses. Moreover, more lanes can be used in the electrophoresis, and sample preparation and sequencing processes can be incorporate in a single apparatus. Research on these techniques is mostly happening in universities.

### *Sequencing by hybridization*

The fundament of sequencing by hybridization is the microarray (DNA chip) technology, which also provides the basis for a huge part of the gene expression analyses in drug development.

In this method, single-stranded sample DNA is hybridized onto a microtechnically created array of DNA oligonucleotide probes. Each base in a sequence is examined by moving the middle base in the oligonucleotide probe to all four probable positions (A, C, G and T), while leaving the rest of the sequence unaffected. The sequence of the DNA is identified according to which of the four oligo probes provides the strongest hybridization signal in each case.





# Training

## *Single molecules detected in real time*

Two strategies currently are present in this area, although these are still far from the step of execution in a practical and marketable form.

1. **Direct observation of nucleotide incorporation:** Here the investigator more or less observes a genetically modified polymerase during synthesis of the second DNA strand. Different fluorescence markers recognize the nucleotide. Problems have been encountered with this method in obtaining adequate signals from individual incorporation events faced with a background of labelled nucleotides and in recognizing all nucleotide incorporation events.

2. **Nanopore-based sequencing method:** Here the DNA is watched during its transfer via pores on the nanometer scale. While the nucleotides cross through the nanopores, the chemical and physical properties of the individual bases are transformed into electrical signals and after that into the sequence – at least that is the hypothesis. We can only guess about the probability of this technology really coming to fruition.

## *Sequencing by synthesis*

Sequencing by synthesis methods can almost be subdivided into two groups: methods that sequence clonally amplified templates and methods that sequence single molecule templates. In both cases, the DNA fragments to be sequenced are physically isolated in a group and subjected to frequent cycles of reagent addition/enzymatic manipulation in order to create the sequences.

## *Sequencing by synthesis of clonally amplified templates*

The majority of cyclic array sequencing technologies are based on sequencing by synthesis, i.e., the gradual constructing of the sequence by a polymerase, related to a detection mechanism. The procedure is based on the clonal amplification of single molecules on beads (microparticles), which are separated in an emulsion, and the consequent massively parallel sequencing of the amplified DNA on the beads positioned in the wells of a PicoTiterPlate™. The detection system of the apparatus is based on the exchange of pyrophosphate – released during the polymerase-catalyzed attachment of a nucleotide to the complementary strand – into light through an enzyme cascade. Below [Figure](#) provides an overview of the process.





# Training

In all the cyclic array methods of this group, the fragments to be sequenced are amplified, either after separation of the molecules (by emulsification or by an acrylamide matrix) or by labelling and consequent isolation of the molecules.

## *Sequencing by synthesis from single molecules*

This sequencing approach presently under development is akin to that of the first group, but with the difference that a more sensitive detection system is required to identify the incorporation of nucleotides into the growing strand.

While all single molecule procedures use the principle of the continuing incorporation of fluorescent nucleotides, they differ in their signal detection systems and the elaborated biochemical aspects.

Table 1. Novel sequencing technologies at a glance.

Technology	Microelectrophoretic sequencing	Sequencing by hybridization	Real-time detection of single molecules	Sequencing by synthesis
<b>Benefits</b>	1) Sequencing with electrophoresis is well recognized 2) Long read widths 3) relatively accurate	appropriate for the resequencing of recognized point mutations	1) appropriate for the identification of single molecules in complex mixtures 2) appropriate for re- and de novo	1) appropriate for the identification of single molecules in complex mixtures 2) appropriate for re- and de novo
<b>Drawbacks</b>	1) Potentially lower output than other methods 2) Possibly not as cost effective as other techniques	1) Narrower read widths in comparison with electrophoretic methods 2) De novo sequencing time-consuming	Not yet commercially available	Narrower read widths In comparison with electrophoretic methods

[Ref: Burkhard Ziebolz and Marcus Droege, Toward a new era in sequencing, *Biotechnology annual review volume* 13, 2007]





# News

## **Mubarak city for scientific research and technology application**

### **Description**

Mubarak City for Scientific Research & Technology Applications (MuCSAT) is the research institutes in Egypt that was concentrating on the development and renewal of industry.

A resolution to build up a science park in the Alexandria region was reached in 1993 in order to gain and improve scientific technologies in various areas of human life. The MuCSAT occupies 250 acres in the industrial district located at New Borg El Arab City, west of Alexandria. This region also inhabits about 40% of the Egyptian industry. The science park composed of 12 research centers to be developed at different times.

### **Goals**

Goals can be summarized as follows:

- Expand centres of scientific Excellency that plan to serve both economic and social developments of the Egyptian society.
- Expand innovative technologies and present new scientific methods in various fields of industry in order to connect research programs to national development plans.
- Offer training consulting and technology transfer to various production and services agents in Egypt.
- Perform applied projects to assure better performance in various areas that can profit the Alexandria region and the national economy.
- Collaboration with various national and international institutes in different areas of technology.

### **Central Labs**

The laboratory was established in 2003 to present its services to the clients in the national market using the most modern standard techniques and methods.

### **Some of the services are mentioned below:**

- Analysis of waste water
- Heavy metal analysis of waste water
- Chemical analysis of drinking water
- Microbiological analysis of drinking water
- Heavy metal analysis of drinking water
- Microbiological screening of companies
- Pesticide analysis in waste and drinking water







# News

## Research centres in Mubarak city are:

- 1) Technological Capabilities Development Centre (TCDC)
- 2) Genetic Engineering & Biotechnology Research Institute (GEBRI)
- 3) Informatics Research Institute (IRI)
- 4) Institute of Advanced Technology & New Materials (IATNM)



Genetic engineering & biotechnology research institute (GEBRI)

## Projects

### Elucidation of Medicinal importance of Egypt Mushroom

The current study intended to grow edible mushroom on industrial and agricultural wastes and production of mushroom mycelia in submerged cultures. In addition the current study aimed to confirm the antitumor activity of mushroom extracts as well as clarifying the modulatory function of these extracts. A possible antitumor activity is reported by mushroom and its extract as indicated by increase in life span of tumoured animals and decrease in tumour growth rate.

### Polymorphism in immunogenetic factors affecting disease outcome in Egyptian HCV Infected Patients

Hepatitis C infection is one of the most important health problems globally. This kind of infection influence large number of Egyptians (~18-24%), in which influence the Egyptian economy in an indirect mode. The mechanism(s) that is responsible in viral clearance, response to treatment, and protection from its related disabilities is not recognized yet. Numerous studies indicated that variations in the immune response, including polymorphisms in the HLA and cytokines genes may affect the result of HCV infection. Also, information regarding these genes involved in variations of the immune response of HCV infected patients with in depth information about HCV genotype, subtypes and viral load will be of immense help in the designing of an efficient vaccine as well as recognition of the type of treatment appropriate to each patient.

[Ref: <http://www.mcsrta.sci.eg/>]





# Trends

## 418 Biotechnology Medicines in Testing Promise to improve treatment for several important diseases:

Millions of people have previously benefited from drugs and vaccines developed through biotechnology and a recent report offers hope that in the future more people will advantage. The report found 418 biotechnology medicines in development for more than 100 diseases. These comprise 210 medicines for cancer, 50 for infectious diseases, 44 for autoimmune diseases, and 22 for AIDS/HIV and associated conditions. These potential medicines, all of which are either in human clinical trials or under review by the Food and Drug Administration, will add to the list of 125 biotechnology medicines previously approved and accessible to patients.

Approved biotechnology medicines previously treat or help avoid heart attacks, stroke, multiple sclerosis, leukaemia, hepatitis, rheumatoid arthritis, breast cancer, diabetes, congestive heart failure, lymphoma, kidney cancer, cystic fibrosis, and other conditions. These medicines depend on many advanced technologies. For instance, most early biotechnology medicines were protein drugs, created by splicing genes into bacteria. They comprise recombinant insulin, human growth hormone, clotting factor for haemophilia patients, and erythropoietin to stimulate the production of red blood cells in kidney dialysis and cancer patients.

An additional kind of biotechnology medicine, the monoclonal antibody, is a laboratory-made version of the naturally happening protein that binds to and neutralizes foreign invaders.

Interferons, proteins that interfere with the capability of a cell to replicate, are the foundation of existing medicines for osteoporosis, chronic granulomatous disease, Genital warts, multiple sclerosis, hairy cell leukaemia and other conditions.

Antisense drugs are medicines that interfere with the communication process that tells a cell to generate an unwanted protein. The first antisense medicine, for the treatment of cytomegalovirus retinitis in AIDS patients, was approved in 1998.

Biotech medicines in development according to therapeutic class

Therapeutic class	Number of medicines
Cancer/associated Conditions	210
Infectious Diseases	50
Autoimmune Disorders	44
AIDS/HIV Infection/associated Conditions	22
Cardiovascular Disease	22
Neurologic conditions	17
Diabetes/associated Conditions	15
Digestive Disorders	14
Respiratory Diseases	13
Blood Disorders	10
Genetic Disorders	9
Skin Disorders	7
Eye Conditions	6
Growth Disorders	4
Transplantation	4
Other	18

\*Some drugs are listed in more than one class





# Trends

The biotechnology medicines now in development make use of these and other high-tech technologies.

For instance, one medicine in the pipeline for rheumatoid arthritis is a recombinant protein that may aid treat autoimmune disorders. Monoclonal antibody medicines in the pipeline are designed to target asthma, Crohn's disease, rheumatoid arthritis, lupus, and different kinds of cancer. Therapeutic vaccines, intended to jump-start the immune system to fight disease, are in development for AIDS and different kinds of cancer. Medicines based on antisense technology are possible treatments for various kinds of cancer, Crohn's disease and heart disease. Gene therapies, which increase normal gene functions or restore or inactivate disease-causing genes, are being examined for several cancers and heart disease.

## Biotech medicines in development according to product class

Drug class	Number of medicines
Monoclonal Antibodies	160
Vaccines	62
Gene Therapy	46
Recombinant	43
Hormones/Proteins	
Cellular Therapy	21
Antisense	20
Interferons	18
Growth Factors	16
Immune-based Therapy	9
Interleukins	8
Others	62

These are only a few examples of innovative ways pharmaceutical and biotechnology companies are fighting disease. The 418 biotechnology medicines in development promise to push the frontiers of science and convey more and better treatments to patients.

[Ref: <http://www.phrma.org/files/Biotech%202006.pdf>]





# Announcements

## BioVisionAlexandria 2008

**From Promises to Practice 12-16 April 2008**

### About the Conference

The Bibliotheca Alexandrina is organizing its fourth international biennial conference, BioVisionAlexandria 2008, held 12-16 April 2008 in Alexandria, Egypt.

As a continuation of the tradition that started in BioVision 1999 in Lyon, the Bibliotheca Alexandrina has been honoured to be an associate with BioVision by which it holds the BioVisionAlexandria every even year alternating with the World Life Science Forum held in Lyon every odd year bringing distinguished speakers in discussions commemorating science and the finest achievements of the human intellect.

The theme of the BioVisionAlexandria 2008 will be "From Promises to Practice" and will focus on translating the best existing knowledge into new approaches. Leading experts of the four corners of the globe are invited to address new approaches explaining why the immense advances that are taking place in science do not adequately translate noticeable improvements in the lives of the poorest 20% of the human race.

Similar to previous BioVisionAlexandria and in BioVision conferences, BioVisionAlexandria 2008 will commence with a Nobel day where eminent Nobel Laureates share their reflections and experience that helped in the advancement of sciences and renovated our world. The Nobel Day is dedicated to honour Nobel Laureates, whose vision and perseverance in the quest for scientific innovation has changed lives and transformed our world.

Followed by the three-day event, the Conference will shed light on themes: Health, Agriculture and Environment. Each of these themes will be addressed by representatives of the greatest minds in industry, science, policymakers and civil society fields.

[Ref:  
<http://www.bibalex.org/bva08/Home/Home.aspx>]





# Cover pictures

## Cover Pictures description (up to down):

### Title:

SNPs: Single Nucleotide Polymorphisms

### Description:

Slight variations in our DNA sequences can have a major impact on whether or not we develop a disease and on our particular responses to such environmental insults as bacteria, viruses, and toxins. They also impact our reactions to drugs and other therapies. One of the most common types of sequence variation is the single nucleotide polymorphism (SNP). SNPs are sites in the human genome where individuals differ in their DNA sequence, often by a single base. For example, one person might have the base A (adenine) where another might have C (cytosine), and so on. Researchers in public and private sectors are generating maps of these sites, which can occur in genes as well as in noncoding regions. Scientists believe such SNP maps will help them identify the multiple genes associated with such complex diseases as cancer, diabetes, vascular disease, and some forms of mental illness. SNP maps provide valuable targets for biomedical and pharmaceutical research.

**Source:** U.S. Department of Energy, Genome Programs. <http://genomics.energy.gov>

### Description:

Front: Scanning electron micrograph of Chinese hamster ovary cells (CHO) following impalement on a nanofiber array. Background: Optical microscope image of a transformed colony of CHO expressing green fluorescent protein from nanofiber delivered plasmids 22 days following impalement upon DNA modified nanofiber array.

This image has been assembled in Adobe Photoshop by overlaying an optical microscope photograph and scanning electron micrograph that has been colorized and manipulated to display perspective.

**Source:** Wikipedia encyclopaedia. [http://en.wikipedia.org/wiki/Main\\_Page](http://en.wikipedia.org/wiki/Main_Page)

### Description:

Crystal structure of a first-generation polyphenylene dendrimer reported by Müllen and coworkers in Chem.-Eur. J., 2002, 3858-3864. Dendritic molecules are repeatedly branched species that are characterized by their structure perfection. The properties of dendrimers are dominated by the functional groups on the molecular surface. Dendritic encapsulation of functional molecules allows for the isolation of the active site, a structure that mimics the structure of active sites in biomaterials because dendritic scaffolds separate internal and external function. It is theoretically possible to design a water-soluble dendrimer with internal hydrophobicity, which would allow it to carry a hydrophobic drug in its interior.

**Source:** Wikipedia encyclopaedia. [http://en.wikipedia.org/wiki/Main\\_Page](http://en.wikipedia.org/wiki/Main_Page)

### Description:

Example of an approximately 37,500 probe spotted oligo microarray with enlarged inset to show detail

**Source:** Wikipedia encyclopaedia. [http://en.wikipedia.org/wiki/Main\\_Page](http://en.wikipedia.org/wiki/Main_Page)

