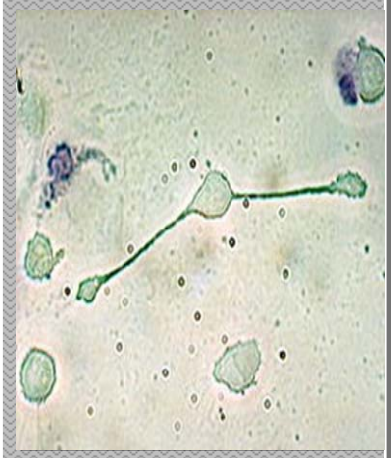

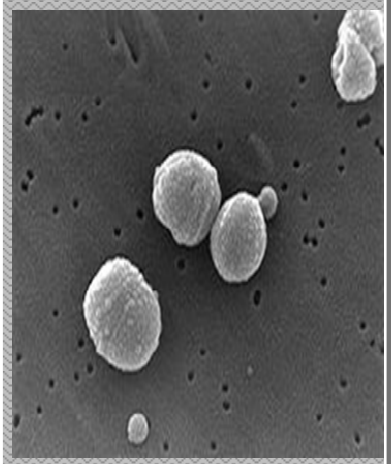

EMGEN Newsletter

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Eastern Mediterranean Health Genomics and Biotechnology Network (EMGEN) was created in 2004 with collaboration of representatives of selected center 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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The identification of the first isolate of influenza B virus using a duplex RT-PCR DNA sequencing in Saudi Arabia (B/Riyadh/01/2007)

Dr. Fahad N. Almajhdi

An article entitled "The identification of the first isolate of influenza B virus using a duplex RT-PCR DNA sequencing in Saudi Arabia (B/Riyadh/01/2007)" aims to development and establishment of a highly specific and sensitive duplex RT-PCT assay for the simultaneous detection and typing of influenza viruses in clinical samples. The study was carried out by Fahad N. Almajhdi; he is working in Department of Botany and Microbiology, Center of Excellence in Biotechnology Research, College of Sciences, King Saudi University, Saudi Arabia; and the paper was published in African Journal of Microbiology Research Vol. 4(9), pp. 697-703, 4 May 2010.

Influenza viruses are single-stranded, negative-sense and segmented RNA viruses that belong to family *Orthomyxoviridae*. Influenza A and B viruses are major causes of highly contagious respiratory disease in young children, the elderly and immunocompromised patients with potential fatal outcomes. They also cause local epidemics and worldwide pandemics with significant infection rates and severe economic losses. Since 2003, only influenza B viruses and two subtypes of influenza A viruses (H1N1 and H3N2) are persistently circulating in the human populations. However, a few subtypes of influenza A viruses like H5N1, H7N3, H7N7, H9N2 and an altered H1N1 (Swine flu) have recently emerged and/or crossed the restrictive species barrier. Since a wide spectrum of pathogens are involved in the acute respiratory disease syndrome of humans, it is important to identify influenza viruses in suspected samples directly and rapidly.

At this moment RT-PCR is well established as the most sensitive and specific technique available for detection of influenza virus infections. Different types and formats have been introduced to enable detection, typing, sub typing and quantification of the virus genome. In Saudi Arabia, influenza viruses, and more specifically influenza B viruses, did not receive much attention in literature. Few reports only described the implication of influenza viruses as important causes of respiratory tract infections among hospitalized children and pilgrims.

A significant lack of information regarding the influenza viruses circulating in Saudi Arabia in terms of prevalent types and subtypes, virulence and risk factors as well as virus diversity/phylogeny still exists and necessitates comprehensive studies.

In the current report, we describe the development of a duplex two-step RT-PCT assay for simultaneous detection and typing of influenza viruses in clinical samples. The test makes use of two primer sets homologous to a highly conserved sequence of the NS-2 gene of each influenza virus type. Different variables of the RT-PCR assay were tested to identify the best possible conditions for getting highly specific, sensitive and reproducible results, including type of reverse transcriptase and polymerase enzymes, buffering system, primer concentration and thermal cycling conditions. The assay specificity was confirmed by parallel testing of influenza A (H1N1) and B viruses with different human respiratory viral agents like Respiratory Syncytial Virus types A and B, Par influenza virus types 2 and 3, Human Corona viruses OC43 and E229, Human Metapneumo viruses, and Measles virus.

The developed assay was applied for analyzing 100 nasopharyngeal aspirate (NPAs) samples collected from young children hospitalized at King Khalid University Hospital (KKUH), Riyadh, Saudi Arabia during the winter season 2007/08. While no influenza A virus was detected, nine samples showed positive reactivity with the influenza B primer set. Recovery of influenza B virus from a representative positive sample was achieved by serial passage in chicken embryos and the virus isolate was designated as Influenza B/ Riyadh/01/2007. The identity of B/Riyadh/01/2007 was confirmed by sequencing of the RT-PCR product and sequence data was submitted to the Gene Bank under the accession number GU135839. Almost a complete homology was recognized with all Influenza B virus strains available on Gene Bank.

In conclusion, the present study describes the development of an accurate and rapid diagnostic approach that detects and differentiates between influenza A and B viruses in a single reaction. We present the first Saudi influenza B virus isolate that was circulating in Riyadh district during the winter season of 2007/08. Antigenic and genomic identification of the isolated Influenza B/Riyadh/01/2007, in particular.

The phylogenetic relationship of HA, NA and MP genes with the different Influenza B virus strains, will provide valuable data that enable recognition of the circulating lineage; identification of possible reassortants and further understanding of the epidemiology and evolution of Saudi strains.

Interview

In this issue, we present an interview with ***Dr. Shahid Mahmood Baig*** *from Human Molecular Genetics group in National Institute for Biotechnology and Genetic Engineering (NIBGE) Faisalabad, Pakistan. He is the head of Health Biotechnology Division and Leader of this group whom we had the following interesting interview with.*

1. Dear Dr. Shahid Mahmood Baig could you please briefly introduce yourself and explain your educational status?

I am currently working as Head of Health Biotechnology Division and Group Leader of Human Molecular Genetics, National Institute for Biotechnology and Genetic Engineering (NIBGE) Faisalabad Pakistan. I completed my M. Sc and M.Phil in Biology from Qauid-i-Azam University (QAU) Islamabad. PhD research was jointly carried out at Department of Molecular Biology and Genetics, Bosporus University, Istanbul Turkey and QAU. Postdoctoral project was undertaken at the Unit of Genetic Engineering, Department of Biochemistry, King Saud University, Riyadh Saudi Arabia (2000-2003). I am also working as Visiting Scientist at the Department of Genetics and Pathology, Rudbeck Laboratory, Uppsala University Sweden and Department of Cellular and Molecular Medicine, Wilhelm Johannes Center, PANUM Institute, Copenhagen University Denmark from the last four years.

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

The main focus of my research is Human Molecular Genetics and by using the modern techniques of molecular biology and biotechnology we localize the disease causing genes and identify the mutations causing genetic diseases in Pakistani families.

3. Why did you choose this field of research?

Due to local tradition of consanguineous marriages in Pakistan, the incidence of various genetic diseases is higher than other populations of the world. β -Thalassemia is the most common genetic disorder in this country. Every year more than 7,000 transfusion dependent children are born in Pakistan. I chose Human Molecular Genetics as a challenge to establish programs for the treatment or prevention/control of genetic disorders in Pakistan through carrier screening, genetic counseling and prenatal diagnosis.

4. Do you apply any biotechnology or genomics tools in your researches and please explain how and where?

We use various techniques of biotechnology and genomics for disease gene mapping, prenatal diagnosis and mutation detection. For prenatal diagnosis we use PCR and automated sequencing whereas for disease gene mapping, a number of techniques including genome wide SNPs analysis, high throughput sequencing, animal model studies, functional and structural analysis are done. Most of the facilities are available at NIBGE and a few techniques are used in the laboratories of our collaborators in Sweden in Denmark by our PhD students who work there as visiting researchers for 6-12 months.

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

We have conventional and real time PCR, cloning, cell culture, animal model, cytogenetic, automated sequencing and LCMS facilities etc., in our laboratory.

6. Are there any biotechnology products that have been made in your country? (I.e. your native researchers involved in the project)

Enzymes of industrial importance like alpha-amylase and beta-glycosidase have been produced by NIBGE Scientists. Similarly, this Institute has also delivered insect and viral resistant, drought and heat tolerant varieties of cotton which are widely cultivated in the country with excellent results.

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

NIBGE has been involved in methanogenesis of agricultural, industrial and solid waste for production of methane gas to convert it into electricity. This product will be commercialized in the near future and it is need of the country due to severe power shortage.

8. Are there significant biotechnology centers in your country?

On paper, there are 27 centers of biotechnology in Pakistan, however, majority of these centers are involved in academic activities. Only 2 or 3 centers are involved in research and development also and focused on production of biotechnology products on commercial scale.

9. Are there any academic training courses in Biotechnology in your country? If yes, to above question, in which level and how many students are trained annually?

The 27 centers of biotechnology in Pakistan are mainly involved in academic activities. In most of centers B.Sc (Hon) in biotechnology is offered. Whereas some institutes like NIBGE offer postgraduate programs in biotechnology i.e. M.Phil and PhD only. Presently, there are about 150 M.Phil and PhD students registered at NIBGE. National and International short training courses and workshops in biotechnology and genetic engineering are also offered on regular basis.

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

Yes, I am familiar with the EMRO countries and EMGEN. The main source of updates is the newsletter and regular announcements on ongoing and future activities of EMRO through emails. Unfortunately, we do not have any active and productive cooperation with the EMRO countries in this area so far. The PhD students from my group have attended three workshops organized in Iran through EMGEN in the last five years.

11. Do you have any suggestions for establishing/extending collaborations with EMRO countries?

A team of active and productive scientist from member states along with world known scientist/s should visit the facilities and assess the potential in member countries. The priority areas must be selected and assigned to the respective member with research grant. A central Institute can be established in any of the member country with consensus and the best scientists from member countries should extend their technical expertise for the establishment of this center. ICGEG is the best model to follow in this regard. Instead of establishing small centers, we must plan for a main Institute or strengthen an already existing one and mobilize the resources and expertise. The regional centers can be established at a later stage when need arises.

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

Yes, we regularly hold national and international short courses and workshops in the field of biotechnology and genetic engineering. The participants from EMRO countries are very welcomed to attend these courses.

13. Do you have any governmental support for biotechnology in your country? And at what level?

There was National Commission of Biotechnology (NCB) for this purpose in Pakistan but it has become non-functional from the last two years due to unavailability of funds. There is no exclusive or dedicated government support for biotechnology in Pakistan. However, competitive research grants for biotechnology and other sciences are available from Ministry of Science and Technology, Higher Education Commission of Pakistan (only for Universities and affiliated Institutions) and Pakistan Science Foundation.

14. What kinds of difficulties do you face, in research and commercialization of medical biotechnology in your country and the region?

The main limiting factor in research is the non availability of funds for medical biotechnology and unscientific attitude and environment at various levels. The cost of production is high due to increasing energy crisis in the country which affects the commercialization of any product in the country and region. Secondly, the availability of low cost imported products in the local market is the main obstacle in this respect.

15. How many trained biotechnologists do exist 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 more than 50 trained biotechnologists in this field and these are also under utilized presently due to prevailing unstable economic crunch and unstable security situation in the country. When situation comes to normal and working environment improves, more trained manpower will be required in this area.

16. Do you have any training courses or workshops in your research centre?

Yes, we do have regular national and international training courses and workshops in our Institute.

17. What is your idea about improvement of linkage between research and industry?

We must follow the successful models of linkage between research and industry of developed countries. The trust and confidence of industry and investor on the local scientist and research institutions is mandatory, which can only be established through proven track record of quality basic and applied research. The industrial sector of the country should also be very well established and flourishing at the same time. Government funded research only can not deliver long term impact on the development of a country.

18. What is your opinion about the development of the biotechnology & genomics in your place?

Being a very big population, Pakistan has a great potential to be a big market for biotechnology products and application of genomics research for treatment and prevention of various diseases. The incidence of genetic diseases is higher in this population as compared to others which emphasize the need for genomic research on indigenous population and production of biotechnology products for targeted and specific treatment. Big populations are always big markets for such products of modern research. Therefore, this population is itself an ultimate big user of its research products. Similarly, production of bio fuel by biotechnology can solve the energy crisis of the country. Plant genomics research undertaken at NIBGE is already helping to improve the yield and quality of cotton in Pakistan.

19. Would you please tell us about the differences of biotechnology and its applications between developed & developing countries? What should we do in this regards?

The major research work and production of biotechnology products is carried out in the developed countries. However, the consumers are more in number in the developing countries due to larger populations, more diseases due to poor health facilities. The local pharmaceutical, seed and pesticide markets have already been captured by the multinational companies of the developed countries. The EMRO countries should seriously identify the products of priority and make a strategy on immediate basis for the production and marketing in the EMRO countries and elsewhere. Sharing of expertise, facilities and resources at this stage is the most important step to convert this dream into reality. The progress in this area is very fast and if we do not join this race now, we will never qualify for this competition.

Thank you Dr. Shahid Baig for sharing information and your opinion with us. Also we are greatful for your kind and useful cooperation.

Biosensor

An investigative tool for the detection of an analyte that combines a biological constituent with a physicochemical detector component is a **biosensor**.

A typical biosensor includes 3 parts:

- *the **sensitive biological element** is the sensitive elements can be shaped by biological engineering (biological substance (e.g. tissue, microorganisms, organelles, cell receptors, enzymes, antibodies, nucleic acids, etc), a biologically derived material or biomimic).*

- *The **transducer** or the **detector element** that transforms the signal resulting from the interaction of the analyte with the biological constituent into another signal (works in a physic chemical method optical, piezoelectric, electrochemical, etc.) and can be more easily deliberate and quantified.*

- *Associated electronics or signal processors that are mainly accountable for the exhibit of the results in a user-friendly way. This sometimes accounts for the most expensive part of the sensor device; however it is possible to make a user friendly display that includes transducer and responsive constituent.*

The blood glucose biosensor is one of the ordinary examples of a commercial biosensor, which to break blood glucose down uses the enzyme glucose oxidase. For this, it first uses two electrons to reduce the FAD (a component of the enzyme) to FADH2 to oxidize glucose. The resulting current is determined of the concentration of glucose. So, the electrode is the transducer and the enzyme is the biologically active component. Lately, arrays of many different detector molecules have been useful in so called electronic nose devices, where the pattern of response from the detectors is used to fingerprint a substance. Recent commercial electronic noses don't have any biological elements.

A canary in a cage, as used by miners to inform of gas, could be measured a biosensor. Today's many of biosensor applications are similar, because they use organisms which respond to toxic substances at much lower concentrations than humans can identify to warn of the presence of the toxin.

Such strategies can be used in ecological monitoring, trace gas detection and in water treatment facilities .

Principles of Detection:

Photometric

A lot of visual biosensors based on the circumstance of surface plasmon resonance are evanescent wave techniques. This utilizes an asset of gold and other materials; especially a thin layer of gold on a high refractive index glass surface can assimilate laser light, producing electron waves (surface plasmons) on the gold surface. This appears only at a specific approach and wavelength of occurrence light and is highly dependent on the surface of the gold, such that binding of a target analyte to a receptor on the gold surface produces an assessable signal.

Surface plasmon resonance sensors function using a sensor chip includes a plastic cassette supporting a glass plate, one side of which is covered with a microscopic layer of gold. This side associates the optical discovery equipment of the tool. Then, the opposite side is contacted with a microfluidic flow system. The contact with the flow system produces channels across which reagents can be approved in solution. This side of the glass sensor chip can be customized in a numeral of ways, to allow easy accessory of molecules of interest. Normally it is covered in carboxymethyl dextran or similar compound.

Do not need total interior reflection geometry in other optical biosensors, and they are mostly based on changes in absorbance or fluorescence of a suitable indicator compound. For example, a fully operational prototype tool to detect casein in milk has been made-up. That is based on detecting changes in absorption of a gold layer. An extensively used research instrument, the micro-array, can also be measured a biosensor.

Biological biosensors often admit a genetically customized form of a native protein or enzyme. The protein is configured to identify a specific analyte and the resulting signal is read by a detection instrument such as a fluorometer or luminometer. Detecting cytosolic concentration of the analyte cAMP is an example of a recently developed biosensor. cAMP is second messenger concerned in cellular signaling triggered by ligands interacting with receptors on the cell membrane. These systems have been created to study cellular responses to native ligands or xenobiotics (toxins or small molecule inhibitors). This term "assays" are usually used in drug discovery progress by pharmaceutical and biotechnology companies. Most cAMP assays in current use need lysis of the cells prior to dimension of cAMP. A live-cell biosensor for cAMP can be used in non -lysed cells with the extra benefit of numerous reads to study the kinetics of receptor response.

Electrochemical

In general, electrochemical biosensors are based on enzymatic catalysis of a response that produces or consumes electrons (they called redox enzymes). The sensor substrate usually consists of three electrodes;

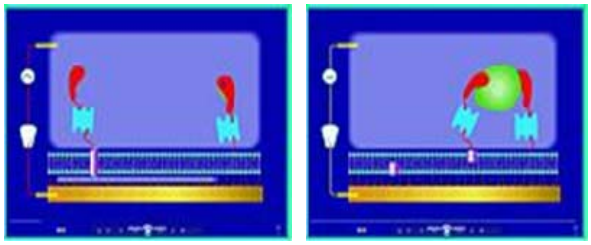
- *Reference electrode*
- *Working electrode*
- *Sink electrode*

An auxiliary electrode (also recognized as a counter electrode) may also be used as an ion source. The target analyte is comprised in the reaction that occurs on the active electrode surface, and the ions produced, make a potential which is debited from that of the reference electrode to give a signal. We can either compute

the current (rate of flow of electrons is now relative to the analyte concentration) at a fixed potential or the potential can be measured at zero current (this gives a logarithmic response). Note that potential of the working or active electrode is space charge sensitive and this is often used. In additional, the label-free and direct electrical discovery of small peptides and proteins is possible by their intrinsic charges using biofunctionalized ion -sensitive field-effect transistors.

Ion Channel Switch

Offering highly sensitive detection of target biological molecules is one of the usages of ion channels An electrical circuit by imbedding the ion channels in supported or tethered bilayer membranes (t-BLM) attached to a gold electrode, is shaped.



CS - channel open **ICS - channel closed**

Apprehension molecules such as antibodies can be bound to the ion channel, so the binding of the target molecule controls the ion flow through the channel. This results in a assessable change in the electrical conduction which is relative to the concentration of the target.

An Ion Channel Switch (ICS) biosensor can be formed by gramicidin, which is a dimeric peptide channel, in a tethered bilayer membrane. One peptide of gramicidin is fixed and one with attached antibody is movable. The magnitude of the change in electrical signal is really increased by separating the membrane from the metal surface using a hydrophilic spacer.

Others

Piezoelectric sensors utilize crystals which undergo an elastic bend when an electrical potential is applied to them. Alternating potential (A.C.) produces a standing wave in the crystal at a characteristic frequency. This frequency is highly dependent on the elastic properties of the crystal, such that if a crystal is covered with a biological recognition constituent the binding of a (large) target analyte to a receptor will create a change in the resonance frequency, which gives a binding signal. In a mode that uses surface audio waves (SAW), the sensitivity is greatly increased. This is a specialized application of the quartz crystal microbalance as a biosensor.

Biosensors on the base of thermometric and magnetic are rare. Connecting the biological elements (small molecules /protein/cells) to the surface of the sensor (metal, polymer or glass) is an important part in a biosensor.

Applications

There are a lot of potential applications of biosensors of various types. The main supplies for a biosensor approach to be valuable in terms of research and commercial applications are the recognition of a target molecule, accessibility of a suitable biological recognition constituent, and the potential for disposable moveable detection systems to be favored to sensitive laboratory-based techniques in some situations.

Some examples are:

- *Glucose detecting in diabetes patients*
- *Other medical health associated targets*
- *ecological applications e.g. the detection of pesticides and river water contaminants*
- *alien sensing of airborne bacteria e.g. in counter-bioterrorist activities*
- *recognition of pathogens*
- *Identifying levels of toxic substances before and after bioremediation*
- *discovery and influential of organophosphate*
- *custom analytical measurement of folic acid, biotin, vitamin B12 and pantothenic acid as an option to microbiological assay*
- *Commitment of drug residues in food, such as antibiotics and growth promoters, mainly meat and honey.*
- *Drug discovery and assessment of biological activity of new compounds.*
- *Protein engineering in biosensors discovery of toxic metabolites such as mycotoxins*

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Pharmacogenomics

One of the branches of Pharmacology which manage the effects of genetic alternation on drug response in patients by correlating gene expression or single-nucleotide polymorphisms with a drug's efficiency or toxicity is **Pharmacogenomics**. By doing so, with respect to the patients' genotype, pharmacogenomics aims to expand balanced means to optimize drug therapy, to confirm maximum efficacy with minimal antagonistic effects. Such approaches assure the advent of "*personalized medicine*"; in which drugs and drug combinations are optimized for each individual's unique genetic makeup.

Pharmacogenomics, which analyze the single gene interactions with drugs, is the total genome application of pharmacogenetics. Doctors are starting to use pharmacogenomic information to advice drugs, but such tests are usual for only a few health problems. However, given the field's rapid growth, for all serious illnesses such as cancer, cardio vascular disorders, HIV, tuberculosis, asthma, and diabetes pharmacogenomics can be used.This new field combines genomics and pharmacology, the science of how drugs work with the science of the human genome.

Drugs have been developed with this idea that each drug working similar in everyone, but genomic study has changed that "one size fits all" advent and opened the door to more personalized advents to using and developing drugs. Depending on the genetic structure, some drugs may work more or less efficiently for some people than the other people. Similarly, some drugs make more or fewer side effects in people than in someone else.

Also Pharmacogenomics may help to save time and money. By using information about genetic structure, researchers may be able to prevent the trial-and-error approach of giving a variety of drugs that are not likely to work for people until they find the right one.

One of the usages of pharmacogenomics is about people who infected with the human immunodeficiency virus (HIV). Before advising the antiviral drug Ziagen, doctors now regularly test HIV-infected patients for a genetic alternative that makes them more likely to have a bad response to the drug.

Another example for pharmacogenomics usage is the breast cancer drug Herceptin. That works only for women whose tumors have a particular genetic outline that leads to overproduction of HER2 protein.

FDA (U.S. Food and Drug Administration) also advocates genetic analyzing before giving the chemotherapy drug Purinethol to patients with acute lymphoblastic leukemia. A genetic variation can be interferes with the ability to process the drug in some people. If the normal dose is adjusted according to the patient's genetic structure, this processing couldn't make severe side effects and amplify risk of infection. The FDA also recommends doctors before administering Composer to examine colon cancer patients for certain genetic variants, which is part of a combination chemotherapy routine. Such patients may require receiving lower doses of the drug because they may not be able to clear the drug from their bodies as quickly as others, resulting in severe diarrhea and increased infection risk.

A great deal research is in progress to find for using drugs to improve human health, how genomic information can be used to expand more modified and cost-effective strategies.

Another active part of pharmacogenomic study is Cancer. For instance, in lung cancer patients whose tumors have a certain genetic modify chemotherapy drugs, Iressa and Tarceva, work much better. On the other hand, research has shown that in the 40 percent of colon cancer patients whose tumors have a significance genetic change, the chemotherapy drugs Erbitux and Vecitibix do not work very well.

For treatment certain mental health disorders such as depression, Pharmacogenomics can be useful to identify the best drugs. Lately, Celexa, which belongs to a widely used class of antidepressant drugs called selective serotonin re-uptake inhibitors (SSRIs), is a genetic variation that influences the response of depressed people. Clinical trials are now in progress to study whether genetic tests that predict SSRI response can improve patients' outcomes.

Pharmacogenomics may also breathe new life into some drugs that were evacuated during the development process. For example, expansion of the beta-blocker drug Gencaro was stopped after two other beta-blocker drugs won FDA acclamation to treat heart failure. But attention in Gencaro revived after tests showed that the drug worked well in patients with two genetic variants that control heart function. Gencaro could become the first new heart drug to need genetic test before recommendation If accepted by the FDA.

Some anticipated benefits of pharmacogenomics;

- ***More Powerful Medicines;*** Pharmaceutical companies will be able to produce drugs based on the proteins, enzymes, and RNA molecules linked with genes and diseases. This will make easy drug discovery and allow drug makers to create a therapy more targeted to specific diseases. This exactness will maximize therapeutic effects and reduce damage to near healthy cells.

- ***Better, Safer Drugs the First Time:*** doctors will be able to analyze a patient's genetic outline and

recommend the best accessible drug therapy from the beginning Instead of the standard trial-and-error tech nique of matching patients with the right drugs. Pharmacogenomics has the potential to decrease the estimated 100,000 deaths and 2 million hospitalizations that happen each year in the United States as the result of unpleasant drug response.

- ***More Accurate Methods of Determining suitable Drug Dosages;*** recent methods on the base of dosages on weight and age will be replaced with dosages based on a person's genetics-how well the body processes the medicine and the time it takes to metabolize it. This will maximize the therapy's value and reduce the probability of overdose.

- ***Advanced Screening for Disease;*** knowing one's genetic code will allow a person to make sufficient existence and ecological changes at an early age so as to prevent or lessen the severity of a genetic disease. Also, advance knowledge of particular disease vulnerability will allow careful monitoring, and treatments can be introduced at the most suitable stage to maximize their therapy.

- ***Better Vaccines;*** Vaccines made of genetic material, either DNA or RNA; assure all the profit of existing vaccines without all the risks. They will activate the immune system and will not be able to cause infections. They will be economical, stable, easy to store, and competent of being engineered to take several strains of a pathogen at once.

- ***Improvements in the Drug Discovery and Approval Process;*** Pharmaceutical companies will be able to find out potential therapies more easily by using genome targets. Beforehand un successful drug candidates may be revived as they are coordinated with the population they serve. The drug support procedure should be facilitated as trials are targeted for particular genetic population groups if greater degrees of success. The cost and risk of clinical trials will be abridged by targeting only those persons competent of responding to a drug.

- ***Decrease in the Overall Cost of Health Care;*** Decreases in the number of unpleasant drug reactions, the number of unsuccessful drug trials, the time it takes to get a drug accepted, the length of time patients are on medication, the number of medications patients must take to find an efficient therapy, the effects of a disease on the body (through early detection), and increase in the range of possible drug targets will encourage a net decrease in the cost of health care. Pharmacogenomics is a youth research. Several of the following barriers will have to be overcome before many pharmacogenomics profit can be realized.

- ***Complexity of finding gene variations that affect drug response;*** when a single nucleotide (A,T,C,or G) in the genome sequence is distorted, Single nucleotide polymorphisms (SNPs) which are DNA sequence variations, will occurs. SNPs occur every 100 to 300 bases next to the 3-billion-base human genome, so millions of SNPs must be recognized and analyzed to find out their involvement (if any) in drug response. Additional complicating the procedure is our limited knowledge of which genes are concerned with each drug response. Because many genes are possible to influence responses, obtaining the big picture on the impact of gene variations is highly time consuming and difficult.

- ***Limited drug alternatives;*** Only one or two standard drugs may be accessible for treatment of a particular state. Patients may be left without any alternatives for treatment if they have gene variations to put off them using these drugs.

- ***Educating healthcare providers;*** Introducing numerous pharmacogenomic products to treat the same state for different population subsets certainly will make difficult the procedure of prescribing and supply drugs. Physicians must perform an extra diagnostic step to conclude which drug is best suited to each patient. To understand the diagnostic precisely and advocate the best course of treatment for each patient, all prescribing physicians, in spite of specialty, will need a better understanding of genetics.

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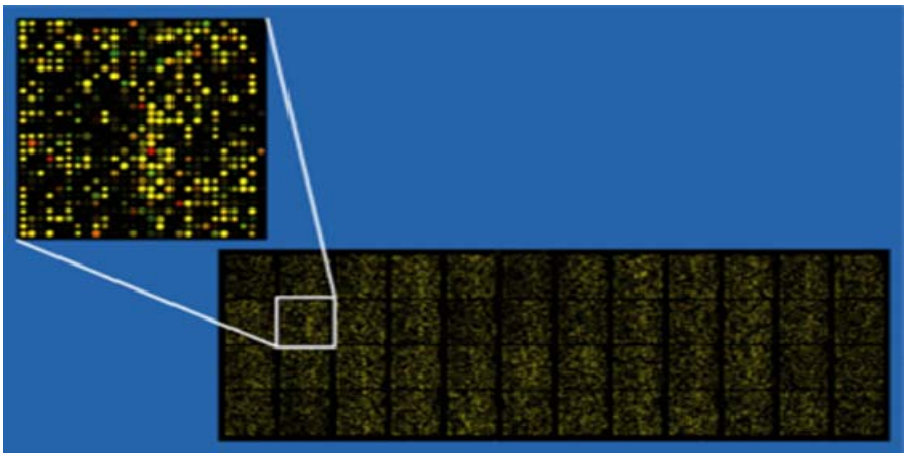
DNA Microarray

One of the complex technologies in molecular biology is **DNA Microarray** which includes of features, "an arrayed sequence of thousands of microscopic spots of DNA oligonucleotides" which consist of micromoles (10^{-12} moles) of a specific DNA sequence, known as *probes*. They can be a small part of a gene or other DNA component that are used to hybridize a cDNA or cRNA sample (called *target*) under high-stringency situation.



Example of an approximately 40,000 probe spotted oligo microarray with enlarged inset to show detail

To find out comparative abundance of nucleic acid sequences in the target, probe-target hybridization is usually discovered and quantified by detection of fluorophore-, silver-, or chemiluminescence-labeled target. Because an array can contain tens of thousands of probes, a microarray investigation can achieve many genetic tests in equivalent. So arrays have radically accelerated many types of study. In typical microarrays ,the probes are closed by the use of surface engineering to a solid surface through a covalent bond to a chemical matrix (via epoxy-silane, amino-silane, lysine, polyacrylamide or others). The solid surface is colloquially known as an *Affy chip* can be glass or a silicon chip. Instead of the large solid support, other microarray platforms, for instance Illumina, make use of microscopic beads. Unlike other types of microarray, DNA arrays use DNA as part of its recognition system or only measure DNA. To expose single nucleotide polymorphisms (SNPs), or to genotype or re-sequence mutant genomes, DNA microarrays can be used to compute changes in expression levels.

Microarrays in addition are differing in manufacture, mechanism, accuracy, efficiency, and cost. Experimental plan and methods of analyzing the data are supplementary factors for microarray tests.

Application

The combination between two DNA strands is The core assumption behind microarrays, the possessions of complementary nucleic acid sequences to specially pair with each other by forming hydrogen bonds between complementary nucleotide base pairs. A high number of complementary base pairs in a nucleotide sequence indicate tighter non-covalent bonding between the two strands. After washing off of undefined bonding sequences, only strongly paired strands will stay hybridized. therefore fluorescently labeled target sequences that attach to a probe sequence make a signal that depends on the power of the hybridization determined by the number of paired bases, the hybridization conditions (such as temperature), and washing after hybridization. Whole power of the signal, from a feature, depends on amount of target sample binding to the probes present on that feature. Microarrays apply relative quantization in which the strength of a feature is contrast to the strength of the same feature under a different state, and the character of the feature is known by its position.

Uses and types

Numerous types of array are present and the broadest difference is whether they are spatially adjusted on a surface or on coded beads:

Two Affymetrix chips

- The conventional solid-phase array is a collection of arranged microscopic "spots", called features, each with a specific probe connected to a solid surface, such as glass, plastic or silicon biochip (usually known as a *genome chip*, *DNA chip* or *gene array*). Most of them can be placed in recognized locations on an exclusive DNA microarray.
- The selection bead array is a collection of microscopic polystyrene beads, each with a defined probe and a ratio of two or more dyes, which do not obstruct with the fluorescent dyes used on the target sequence.

DNA microarrays can be used to identify DNA (as in comparative genomic hybridization), or detect RNA (usually as cDNA after reverse transcription) that could or could not be translated into proteins. Expression analysis or profiling is the methods of measuring gene expression by cDNA.

Application

- ***Gene expression profiling:*** To consider the effects of assured treatments, diseases, and developmental stages on gene expression in mRNA or gene expression profiling research, expression levels of thousands of genes are coinciding detected. For instance, to recognized genes whose expression is distorted

in response to pathogens or other organisms by comparing gene expression in infected to that in uninfected cells or tissues microarray-based gene expression profiling can be used.

- ***Comparative genomic hybridization:*** appraising genome content in assorted cells or closely connected organisms.

- ***GeneID:*** checking IDs of organisms in food and nourish (like GMO), mycoplasms in cell culture, or pathogens for disease exposure, with small microarrays, usually PCR and microarray technology should be combined.

- ***Chromatin immunoprecipitation on Chip:*** immunoprecipitating particular protein (ChIP) could isolate DNA sequences bound to that protein, then these fragments that can be hybridized to a microarray (such as a tiling array), approving the determination of protein binding site occupancy all over the genome. histone modifications (H3K27me3, H3K4me2, H3K9me3, etc.), Polycomb-group protein (PRC2:Suz12, PRC1:YY1) and trithorax-group protein (Ash1) are the example proteins to immunoprecipitate for studying the epigenetic landscape or RNA Polymerase II or the transcription landscape.

- ***DamID:*** Analogously to ChIP, genomic regions bound by significance protein can be remote and used to probe a microarray to determine binding site occupancy. ChIP and DamID which does not require antibodies, make adenine methylation near the protein's binding sites to selectively amplify those regions, and introduced by expressing minute amounts of protein of interest compound to bacterial DNA adenine methyltransferase.

- ***SNP detection:*** distinguishing single nucleotide polymorphism among alleles inside or between populations. Genotyping, forensic analysis, calculating predisposition to disease, identifying drug-candidates, evaluating germline mutations in individuals or somatic mutations in cancers, assessing loss of heterozygosity, or genetic linkage analysis are several applications of microarrays that make use of SNP discovery.

- ***Alternative splicing detection:*** An '*exon junction array* conceive uses probes defined to the predictable or possible splice sites of certain exons for a gene. Analyzing the expression of option splice forms of a gene is one of its usages. Employing probes designed or predicted genes shows that exon

arrays have different design, and can be used for detecting different splicing isoforms.

- ***Fusion genes microarray:*** detecting fusion transcripts, *e.g.* from cancer specimens. The assumption behind this is structure on the alternative splicing microarrays. The oligo design policy enables combined measurements of chimeric transcript junctions with exon-wise measurements of individual fusion partners.

- ***Tiling array:*** Genome tiling arrays add up to overlapping probes designed to thickly represent a significance genomic region, sometimes as large as whole human chromosome. To empirically identify expression of transcripts or alternatively splice forms which may not have been before recognized or predicted is the purpose.

- ***Expanding a new molecular classification of cancer :*** as well as clustering of cancers according to prognostic groups on the base of gene expression profiles such as breast cancer

Fabrication

Depending on the number of probes under examination, costs, customization supplies, and the type of scientific question being asked microarrays can be artificial in different ways. Arrays may have as few as 10 probes or up to 2.1 million micrometre-scale probes from commercial vendors.

Spotted vs. in situ synthesized arrays

Microarrays can be made-up via a variety of technologies, including printing with fine-pointed pins onto glass slides, photolithography using pre-made masks or dynamic micromirror devices, ink-jet printing, or electrochemistry on microelectrode arrays.

oligonucleotides, cDNA or small fragments of PCR products that correspond to mRNAs are the probes of *spotted microarrays* . The probes are synthesized previous to statement on the array surface and are then "spotted" onto glass.

In *oligonucleotide microarrays*, the probes are small sequences designed to compatible parts of the sequence of recognized or predicted open reading frames. This term most often allude to a particular method of fabricate while oligonucleotide probes are often used in "spotted" microarrays.

Two-channel vs. one-channel detection

Two samples to be compared (e.g. diseased tissue against healthy tissue) and that are labeled with two different fluorophores preparing cDNA which is normally hybridized with ***Two-color microarrays*** or ***two-channel microarrays***.

In ***single-channel microarrays*** or ***one-color microarrays,*** the arrays supply strength data for every probe or probe set conveying a relative level of hybridization with the labeled target. However, they do not actually indicate abundance levels of a gene but rather relative abundance when compared to other samples or conditions when processed in the same trial.

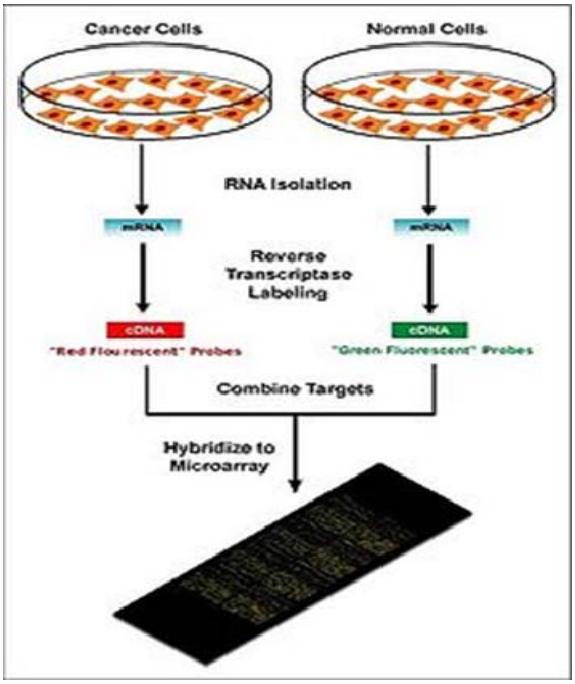


Diagram of typical dual-color microarray experiment

Microarrays and bioinformatics

Gene expression principles from microarray experiments can be represented as heat maps to imagine the result of data analysis.

The beginning of cheap microarray experiments produced several specific bioinformatics challenges:

- *the numerous levels of duplication in experimental design (Experimental design)*
- *the number of dais and independent groups and data arrangement (Standardization)*
- *the dealing of the data (Statistical analysis)*
- *correctness and exactitude (Relation between probe and gene)*
- *the pure volume of data and the ability to split it (Data warehousing)*

References:

1- http://en.wikipedia.org/wiki/Microarray

2- P. F. Macgregor, J. A. Squire, Application of Microarrays to the Analysis of Gene Expression in Cancer, *Clinical Chemistry;*(2002) 48: 1170-1177.

3- D. J. Brennan, S. L. O'Brien, A. Fagan, A. C. Culhane, D.G. Higgins, M. J. Duffy, W. M. Gallagher, Application of DNA microarray technology in determining breast cancer prognosis and therapeutic response. *Expert Opin Biol Ther*.(2005); 5(8):1069-83.

Early Development of Anti-HIV Neutralizing Antibodies

Initializing broadly reactive neutralizing antibodies (NAbs) are the major step towards developing effective vaccine against HIV. By binding to the surface of the HIV, these antibodies prevent the healthy cells to be infected. Not all of the people are capable of producing bNAbs, which is the effective antibody against HIV. The researchers are trying to develop and extract this antibody for future vaccination of the entire people that might be in the risk.

Stamatatos and his team at the Viral Vaccines Program at Seattle BioMed have revealed that only 30% of infected population is capable of developing develop broadly-reactive neutralizing antibodies. These people have healthier and stronger immune system. Moreover, the above mentioned antibodies are developing after about a year of getting infected, which is quicker than previously believed.

Scientists are trying to understand the stochastic process behind production of these antibodies. This will help them to produce the targeted vaccine.

Reference:

Iliyana Mikell, D. Noah Sather, Spyros A. Kalams, Marcus Altfeld, Galit Alter, Leonidas Stamatatos. Characteristics of the Earliest Cross-Neutralizing Antibody Response to HIV-1. *PLoS Pathogens*, 2011; 7 (1): 1-15.

'Longevity' Protein SIRT1 May Ward Off Precursor to Prostate Cancer

"Longevity" protein SIRT1 can suppress prostatic intraepithelial neoplasia (PIN), which is a known precursor to prostate cancer. Researchers from the Kimmel Cancer Center at Jefferson and two other institutions have found that deletion of the Sirt1 gene in mice resulted in PIN formation .

Fifteen years of research on the SIRT1 has showed that this gene inhibits tumor growth in certain cancers and promote it by inactivating the tumor suppressor. This gene role in the development of androgen-responsive tissues, such as the prostate has been carried out as a genome-wide microarray, pathway analysis and histology on Sirt1 positive and negative transgenic mice and littermate controls. Dr. Pestell‘s data show that drugs that activate Sirt1 could block prostate cancer. This result could finally lead to production of anti-prostate cancer drug.

Reference:

http://www.ScienceDaily.com

New Therapies for Prevention and Treatment of Alzheimer's Disease Identified

Researchers at Blanchette Rockefeller Neurosciences Institute (BRNI) have investigated the role of the synapses lost in Alzheimer's Disease before the plaques and tangles development. BRNI's new therapeutics prevents the progressive symptoms of Alzheimer's Disease by preventing the loss of synapses.

Alzheimer's Disease is a disease of synapses. So, by preventing the loss of the synapses, Dr. Daniel Alkon and colleagues' study have found the great progress towards elimination of this dangerous disease. The study on mice, treating them with Bryostatin, which independently path the creation of synapses at the molecular level, demonstrated that this pharmaceutical compounds promoted the growth of new synapses and preservation of existing synapses. The future study on these synaptogenic compounds for production of an effective drug against Alzheimer will be shortly started.

Reference:

Jarin Hongpaisan, Miao-Kun Sun, and Daniel L. Alkon. PKC ε Activation Prevents Synaptic Loss, Aβ Elevation, and Cognitive Deficits in Alzheimer's Disease Transgenic Mice. *Journal of Neuroscience*, 2011; 31: 630-643

Embryonic Stem Cells Help Deliver 'Good Genes' in a Model of Inherited Blood Disorder

A new gene therapy strategy has been reported by Researchers at Nationwide Children's Hospital for treating beta-thalassemia blood disorder. This new gene correction approach involves of parthenogenetic stem cells which has some advantages: the recipient's immune system may potentially not view them as foreign, and they contain only a single set of the genetic information instead of the double set present in body cells, they may not contain certain abnormal genes present in the other copy. The affected person has two copies of the gene: one defective and one normal copy. Therefore, researchers using unfertilized eggs from afflicted mice to produce a batch of embryonic stem cell lines. These cells do not contain the affected gene, and can be used for transplantation-based treatments of the same mice. These results will also help finding new treatment strategies for tuberous sclerosis or Huntington's disease.

Reference:

Sigrid Eckardt, N. Adrian Leu, Ashley Yanchik, Seigo Hatada, Michael Kyba and K. John McLaughlin. Gene therapy by allele selection in a mouse model of beta-thalassemia. *Journal of Clinical Investigation*, 2011, 121(2): 623-627.

Pakistan Biotechnology Information Center (PABIC)

At present, there are several reputable institutions working on various aspects of biotechnology in Pakistan, one of them is the Pakistan Biotechnology Information Center (PABIC) (http://www.pabic.com.pk) that was constructed at Latif Ebrahim Jamal National Science Information Center, University of Karachi under the supporting of International Service for Acquisition of Agri-Biotech Applications (ISAAA) and National Commission on Biotechnology. An attempt to begin multidisciplinary research and improve the awareness and appreciation of biotechnology at the local and international levels is the ambition of constitute of Pakistan Biotechnology Information Center.

However there is a serious lack of appreciation of biotechnology at the public and industrial levels in Pakistan. Organization and exchange of information between institution and practitioners of biotechnology is less than sufficient. Therefore, there is a need of a resource center in Pakistan, which can serve as a core to distribute information, to support the collaborative efforts and to develop a institutions and individuals working in this field.

Aims and Objectives:

To initiate of Biotechnology based information programs.

- *To create awareness in public, education and industrial division.*
- *To provide first time learning services using the latest learning technologies that can be emulated by educational institute.*
- *To distribute of information.*
- *To exchange ideas appertaining to sensible use of biotechnological novelty.*
- *To educate and elevate awareness about the biotechnology.*
- *To clarity on presenting / discussing key issues affecting the industry.*

There are several universities and research institutes included in this organization:

*** H. E. J. Research Institute of Chemistry (H. E. J. R. I. C), University of Karachi, Karachi.**

- *Medicine*
- *Transgenic Plant Technology*

*** Center for Molecular Genetics (CMG), University of Karachi, Karachi.**

*** Center of Excellence in Molecular Biology (CEMB), University of Punjab, Lahore**

- *Transgenic Plant Technology*
- *Environmental Biotechnology*
- *Health & Medical Diagnostics*
- *Basic Research*
- *Production Activities*

*** Institute of Agricultural Biotechnology And Genetic Resources (NIABGR) NARC, Islamabad**

*** National Institute for Biotechnology and Genetic Engineering, (NIBGE) Faisalabad**

- *Commercial Activities In Tissue Culture*

*** Biomedical & Genetic Engineering Division, Dr. A. Q. Khan Research Laboratories, Islamabad.**

*** Institute of Biotechnology and Genetics Engineering, (IBGE) NWFP Agriculture University , Peshawar**

*** Ayub Agriculture Research Institute, (AARI) Faisalabad.**

*** Nuclear Institute for Agriculture Biology (NIAB) Faisalabad.**

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Announcement

http://www.pasteur.fr/stemcell2011

THEME OF THE CONFERENCE

Stem cell biology progresses very rapidly, in terms of identification of stem cells, their basic biology and role in development and regeneration. Unraveling these mechanisms leads to new concepts and strategies for clinical intervention, including disease modeling, drug screening, and cell therapy. The conference will bring together experts in basic research, with stem cell biologists grappling with the complexity of cell fate determination, bioimaging, and those using stem cells in patients.

http://www.hgm2011.org

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Deputy Ruler of Dubai, UAE Minister of Finance,
President of the Dubai Health Authority,
Patron of the Award for Medical Sciences.

Announcement

http://www.acmgmeeting.net

2011 ACMG Annual Clinical Genetics Meeting
March 16-20, 2011 * Vancouver, British Columbia, Canada

Advance Discount Registration Deadline: February 9, 2011

About the Meeting

The ACMG meeting is THE educational and networking event for medical and clinical geneticists, genetic counselors, pediatric and obstetric practitioners who are providing comprehensive diagnostic, management and counseling services for patients with, or at risk for, genetically influenced health problems; laboratory directors and technicians conducting genetic testing; researchers involved in the discovery of genetic disorders and treatments; and all healthcare and public health professionals with an interest in the rapidly evolving field of medical genetics and its integration into healthcare.

The celebration of ACMG's 20th Anniversary, the presentation of cutting-edge science, practical medical and clinical applications, and the latest research, combined with networking opportunities and the spectacular destination, put the ACMG Annual Clinical Genetics Meeting on the list of scientific meetings you cannot afford to miss in 2011!

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NOTE: Please contact our office if you would like to submit a late breaking abstract at abstracts@keystonesymposia.org or 800-253-0685.
There is a $50 late fee for any abstract processed after the abstract deadline.

Announcement

http://www.icbbt.org

2011第三届生物信息与生物医药技术国际会议 (ICBBT 2011)

Introduction

The aim objective of the International Conference on Bioinformatics and Biomedical Technology (ICBBT) is to provide a platform for researchers, engineers, academicians as well as industrial professionals from all over the world to present their research results and development activities in Bioinformatics and Biomedical Technology. Previous ICBBT 2009 and ICBBT 2010 were held in Singapore and Chengdu respectively.

IACSIT
WWW.IACSIT.ORG

CBEES
www.cbees.org

http://www.cs.gsu.edu/isbrall/

7th International Symposium on Bioinformatics Research and Applications

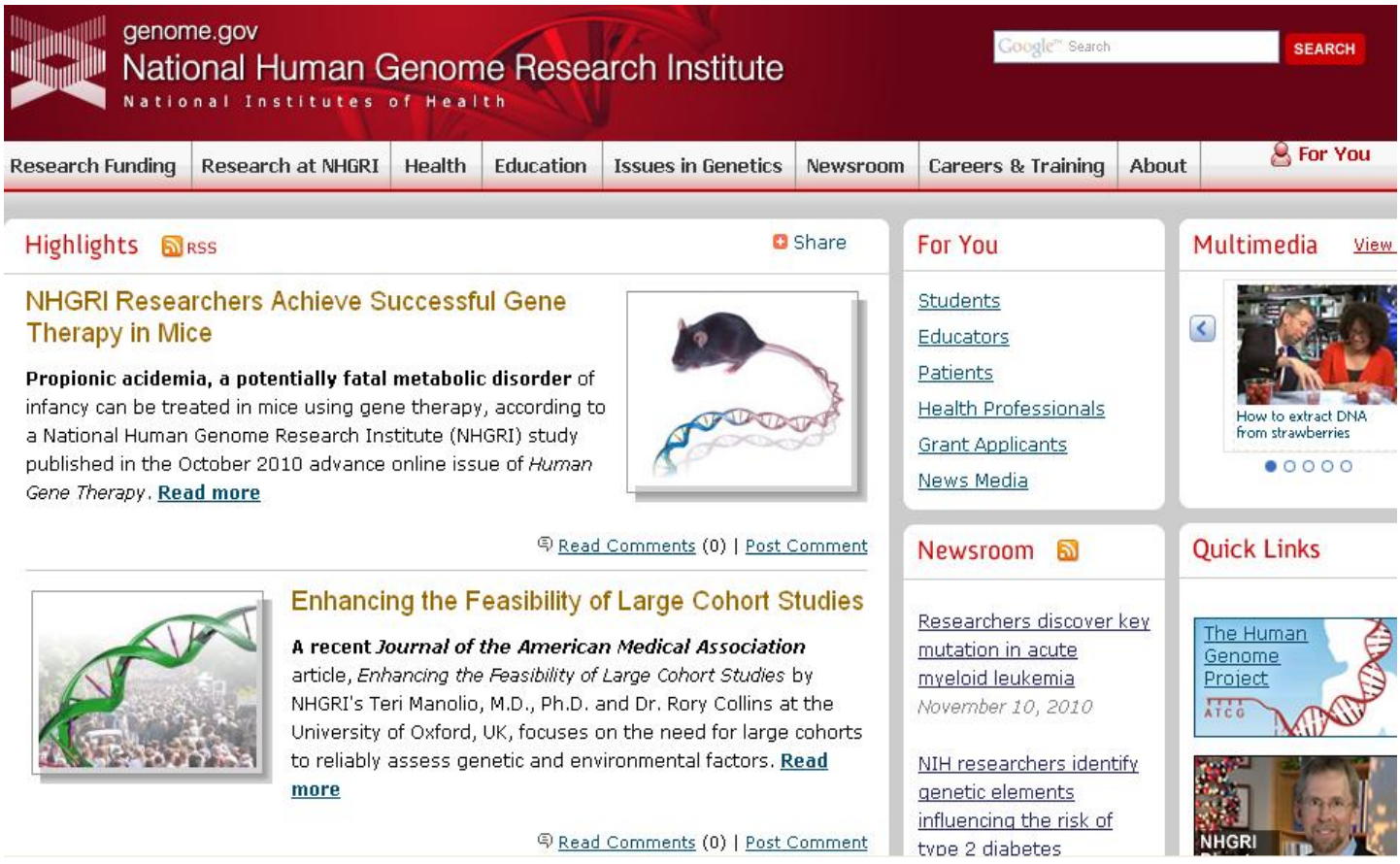
ISBRA 2011, Central South University, China

Paper Submission
Feb 11, 2011

National Human genome Research Institute

In this issue, we would like to introduce National Human Genome Research Institute website (http://www.genome.gov), which was established in 1989 to carry out the role of the National Institutes of Health (NIH) in the International Human Genome Project (HGP). This website is a very useful portal, which consist of nine different information sections:

- *Research Funding*
- *Research at NHGRI*
- *Health*
- *Education*
- *Issues in Genetics*
- *News room*
- *Careers and Training*
- *About NHGRI*
- *For you*



Research Funding section contains interesting information about (HGP), ENCyclopedia of DNAElements, International HapMap Project, Population Genomics, The Cancer Genome Atlas (TCGA) and The Knockout Mouse Project.

Intramural Research Division in NHGRI, conducts a widea range of laboratory and clinical research programs.

The next section is "***Health***", gives the information about genetics and genomics, rare diseases, patient care and more, is divided into two groups;

- *For Patients and the Public*
- *For Health Professionals*

Education section is about educational materials about genetics and genomics.

You can read all about policy, legal and ethical issues in genetic research in ***Issues in Genetics*** section.

Latest news, media resources and information from NHGRI are available at the ***News room.***

NHGRI has provided quality recruitment and job seeking opportunities for professionals in the Genetics and genomics research, you can find everything about Education, training, professional development and career opportunities at NHGRI in ***Careers and Training*** section.

One of the most useful link in this site is ***For You*** section, this section has specialized information for students, educators, patients and health professionals.

Cover Picture

Title: *Macrophages*

Macrophages are white blood cells within tissues, produced by the differentiation of monocytes. Human macrophages are about 21 micrometers (0.00083 in) in diameter. Monocytes and macrophages are phagocytes, acting in both non-specific defenses (innate immunity) as well as to help initiate specific defense mechanisms (adaptive immunity) of vertebrate animals. Their role is to phagocytose (engulf and then digest) cellular debris and pathogens either as stationary or as mobile cells, and to stimulate lymphocytes and other immune cells to respond to the pathogen. They can be identified by specific expression of a number of proteins including CD14, CD11b, F4/80 (mice)/EMR1 (human), Lysozyme M, MAC-1/MAC-3 and CD68 by flow cytometry or immunohistochemical staining. They move by action of amoeboid movement.

Source: *http://www.wikipedia.org*

Title: *Chemiluminescence of Luminol*

Chemiluminescence is the emission of light by a chemical reaction. Some enzyme reactions produce light and this can be measured to detect product formatiohn. These types of assay can be extremely sensitive, since the light produced can be captured by photographic film over days or weeks, but can be hard to quantify, because not all the light released by a reaction will be detected. The detection of horseradish peroxidase by enzymatic chemiluminescence (ECL) is a common method of detecting antibodies in western blotting. Another example is the enzyme luciferase, This is found in fireflies and naturally produces light from its substrate luciferin.

Source: *http://www.wikipedia.org*

Title: *SEM micrograph of Streptococcus. pneumoniae.*

Streptococcus pneumoniae, or **pneumococcus**, is gram-positive, alpha-hemolytic, bile-soluble aerotolerant anaerobe and a member of the genus *Streptococcus*. A significant human pathogenic bacterium, *S. pneumoniae* was recognized as a major cause of pneumonia in the late 19th century and is the subject of many humoral immunity studies. Despite the name, the organism causes many types of pneumococcal infection other than pneumonia, including acute sinusitis, otitis media, meningitis, bacteremia, sepsis, osteomyelitis, septic arthritis, endocarditis, peritonitis, pericarditis, cellulitis, and brain abscess.*S. pneumoniae* is the most common cause of bacterial meningitis in adults, children, and dogs, and is one of the top-two isolates found in ear infection, otitis media.

Source: *http://www.wikipedia.org*