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Newsletter

Center of

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feedback from participants.

Applications of DNA Sequencing

A four-day workshop and training program in DNA sequencing using the Applied Biosystems (HITACHI) 3130 Genetic Analyzer was successfully organized between 30.10.2010 and 2.11.2010 at the CEGMR/DGMU attended by a number of participants from King Abdulaziz University and elsewhere. The program was announced well ahead of the scheduled date and is CME accredited by the Saudi Health Commission with 15 credit hours. A number of senior staff members were involved in the theoretical and practical aspects of the workshop.

CEGMR Administrative Staff Qualified Global Leadership



As part of the continuous endeavor to develop its leadership's qualities, the CEGMR has great pleasure in announcing the successful completion by its management team of the LMI international management leadership courses. Dr. Mohammed Al-Qahtani, Director CEGMR, Dr. Adel Abuzenadah, Vice-Director for Administrative Affairs, Dr. Adeel Chaudhary, Vice-Director for Technical Affairs and Dr. Mamdooh Gari,

Head of the continuous education, all undertook the courses and passed with flying colors.

The LMI courses covered topics such as personal productiveness, personal leadership, as well as strategic leadership and management. All of the aforementioned members were honored to receive a commemorative comprehensive leadership shield to mark their achievement during the celebration held on the 1st June 2010 at which the King Abdulaziz University also received a commemorative shield for excellence in administrative leadership programs. The CEGMR staff extends its deep appreciation and congratulation for this achievement and is proud to work with an excellent management team with a strong vision for a brighter future.

CEGMR Research Developments

Neurogenetic Disease Research Group Progress Report



At CEGMR, Neurogenetic Disease Research Group (NDRG) is headed by Dr. Adeel G Chaudhary whose team currently seeks to investigate the genetic profiling of common neuromuscular dystrophy in Saudi Arabia. The overall goal of the program is to address the most common neuromuscular disorders such as Duchenne Muscular dystrophy (DMD), Spinal Muscular Atrophy (SMA), and Myotonic Dystrophy in the Western region of Saudi Arabia. Research at CEGMR has certainly





moved from the Multiplex PCR diagnostic approach to the more comprehensive diagnosis using the MLPA technique for screening of the large Dystrophin gene for deletions/ duplications that have not been detected previously. The NDRP group aims to use the high throughput techniques such as SNP microarray and next generation sequencing for the search of candidate gene defects in the wide spectrum of neuromuscular disorders in future. The group has reported the following research developments till date:



Collaborations with King Khalid National Guard Hospital, King AbdulAziz University Hospital and the Saudi-German Hospital have been established. Families with affected children were referred to the CEGMR and blood samples have been collected with informed consent of the subjects. The spectrum of deletion in the dystrophin gene has been defined in 34 subjects using Multiplex PCR as a provisional diagnosis. Establishment of the SALSA-MLPA technique has been achieved during the course of this project and has been useful for the detection of deletion in patients and detection of carriers among female relatives.

The work has been extended to the molecular diagnosis of another type of neuromuscular disorders: the spinal muscular atrophy (SMA). In future the potential of comparative genomic hybridization (CGH) will be utilized to characterize the disease. The expectation is that novel deletions will be identified during the process since CGH covers all the chromosomes in a single run. The team is encouraged to extend the research work further according to the initial proposal in addition to floating side-projects.

Upcoming Events

First International Genomic Medicine Conference in Saudi Arabia

The date for the first international genomic medicine conference in Saudi Arabia organized by the CEGMR has been announced by the Director of CEGMR Dr. Mohammed Hussein Al-Qahtani. The conference will take place at the King Fahad Medical Research Center auditorium on the 16 and 17 February 2011.

Distinguished international speakers will take part and provide their research insights. Various workshops dealing with hands-on training in next generation sequencing, gene expression analysis using the affymetrix platform, array CGH using the Agilent platform and techniques related to molecular diagnostics of the DGMU will be other highlights of the conference. Under the supervision of Ms. Reem Mohammed Bashmail, the CEGMR IT staff has uploaded all the details of the conference on the CEGMR website.

Dr. Al-Qahtani directed all the CEGMR staff to accomplish assigned tasks to make the conference a success.











INTERNATIONAL SPEAKERS



Prof. Eamonn Maher

Professor of Medical Genetics Department of Medical and Molecular Genetics titute of Biomedical Research Iniversity of Birmingham



Dr. Ioannis Ragoussis

Head of Genomics Wellcome Trust Centre for Human Genetics, University of Oxford



Dr. Fahd Al-Mulla

ciate Professor lead of Molecular Pathology aculty of Medicine. await University, Kawait



Prof. Adrian Harris

rofessor of Medical Oncology Director Cancer Research UK Molecular Oncology Laboratories Vestiberall Institute of Molecular Medicine Iniversity of Oxford, UK



Dr. Luke Hesson

Team Leader & Lectures Adult Cancer Program, Cancer Institute New South Wales, Australia



Prof. Lotfi Chouchane

rolessor of Genetic Medicine and Immunology. sistant Dean for Busic Scien Neill Cornell Medical College, Quar.



Prof. Ghulam Mufti

rolessor of Haemato-oncology, lead of department and Clinical Director repartment of Hematological Medicine ting's College, UK



Prof. Shiekh Riazuddin

Professor of Haemato-oncology. Head of department and Clinical Director Department of Hematological Medicine



Dr. Daniel Peterson



Prof. Vladimir Bajic

or, Computational Bioscience Research enter rofessor. Applied Mathematics and omputational Science AUST, Saudi Arabia



Dr. Joyce Harper

Reader in Human Genetics and Embryology UCL Centre for PG&D University College London, UK



Dr. Wael Kafienah





KING ABDULAZIZ UNIVERSITY - JEDDAH

16 - 17 February 2011 Main Auditorium, King Fahad Medical Research Center King Abdulaziz University





PROGRAM AT GLANCE

Cancer Genomics

-Notch Signalling: New Pathways and Mechanisms in Tumour Angiogenesis and Targets for Therapy.

-Leukemia Oncogenesis and the use of Next-Generation Sequencing

Cancer Epigenomics

-miRNA Expression as Independent Prognostic Markers in Breast Cancer. Genome-wide Methylation Profiling of Laterally Spreading Colon Cancer using Next-Generation Sequencing.

Cancer Research in the Arabian Gulf

-Genomics of Breast Cancer: Preventive and Predictive Medicine Implications.
-Raf Kinase Inhibitor Protein (RKIP): A Novel 'Gate keeper' and 'Caretaker'

Inherited Genetic Disorders: Examples & Impact

-Medical and Biological insights from Genetic Studies of Inherited Rare Diseases
-Molecular & Genetic Basis of Hearing Impairment

Pre-Implantation Genetics: Updates & New Challenges

-What is new in Preimplantation Genetic Diagnosis (PGD)? -PGD in Saudi Arabia

The Promise of Stem Cell Therapy

 Utilizing Genetic Regulation of Stem Cell Fate for Regenerative Therapies
 Stem Cells and Skeletal Tissue Engineering: Saving Knees and Saving Lives!

The Power of Bioinformatics

-Knowledge extraction and integration of information from biomedical repositories

Workshops:

- ♦ Whole-genome DNA Sequencing
- Comparative Genomic Hybridization (CGH) for Disease Characterization
- High-density Arrays for Whole-genome Expression Analysis
- ◆ Advanced Molecular Diagnostic Tools & Applications



Conference

15

online registration: http://cegmr.kau.edu.sa

for further information Fax: +966-2-6400000 Ext. 52521 Phone: +966-2-6400000 Ext. 25973



Promotional Foreign Visit

CEGMR staff get training on comparative genomic hybridization in Germany



In continuation of the 'researcher education and training' program, the Director of CEGMR, Dr. Mohammed Hussein Al-Qahtani yet again organized a comprehensive training program at the Agilent's array manufacturing site in Waldbronn in Germany. The training took place at a leading application support center in Waldbronn, Germany which hosts such advanced courses. Dr. Peer Zada and Ms. Maha Alquaiti from the CEGMR participated in the extensive week long training program for the comparative genomic hybridization (CGH) on the Agilent's high resolution array scanner.

The comprehensive course involved hands-on instrument training sessions as well as application-based courses on a variety of related topics. Hands-on lab experience with Agilent's array scanner and software was part of the program.

The course started with an overview of the array CGH on a high resolution scanner. This was followed by other topics that included an overview of instrument operation and hardware, various sample preparation

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Designer

Reem Mohammed Bashmail

methods and their use in CGH, library preparation, strategies for labeling of genomic DNA, microarray processing including hybridization and feature extraction troubleshooting, and analysis software. Detailed overview of the system chemistry will enable better handling of the system and troubleshooting in case of any eventual need in-house



at the CEGMR. The course also included classroom and laboratory sections for fragment and library construction as well as information and strategies for different CGH applications. Application of the Agilent's array scanner in terms of microRNA expression analysis was also discussed during the course.

Dr. Peer Zada who was very much delighted upon successful completion of the course elaborated on the diagnostic potential of CGH arrays in various genetic diseases. "Array CGH has the potential to map DNA copy number changes to positions in the genome and has a number of advantages over expression arrays", he added. Copy number changes contribute to tumorigenesis and their characterization using CGH, for example, becomes essential for both the basic understanding of cancer and its diagnosis in







addition to its use in genetic diseases. The Agilent array scanner was accrued by CEGMR as part of its 'advanced technology' expansion drive. The Director of CEGMR, Dr. Al-Qahtani stressed on the need to train the CEGMR staff with this technology. Dr. Al-Qahtani wished Dr. Peer Zada and the CGH team success in their research pursuits and reiterated their commitment to research in a highly professional manner.

Personalized Medicine:

Dream Comes True, CEGMR Team Wins Competition

CEGMR team comprising of the Director, Dr. Mohammed Hussein Al-Qahtani; the Vice-Director for Technical Affairs, Dr. Adeel Gulzar Choudhary; the Vice-Director for Financial Affairs, Dr. Adel Abuzenadah; the Head of CEGMR Education and Outreach Program, Dr. Mamdooh Abdullah Gari; Dr. Ashraf Dallol and other research staff have won this year's competition to establish a new Center of Innovation in Personalized Medicine with a budget exceeding 50 million Saudi Riyal spanning over a period of five years. The competition was part of the Technology Innovation Center (TIC) program developed and announced by the King Abdulaziz City for Science and Technology (KACST) in Autumn 2009 under the directives of the royal order in order to create a series of university-based industry collaborative research centers at carefully selected locations in the Kingdom.





Immediately following the initial announcement for the TIC, the Center submitted six 'letters of intent' to the KACST covering research areas where CEGMR has recognized a certain demand to strengthen the overall capacities in its broader field of operation.

Among these, 'Center of Innovation in Bioinformatics and Computional Biology (CIBCB)', 'Center of Innovation in Personalized Medicine (CIPM)', 'Innovation Center for Regenerative

Medicine (ICRM)', 'National Innovation Center for Biobanking (NICB)' were approved by the KACST committee for a full proposal submission. The inaugural round of the proposal review process eventually culminated in the short listing of CIPM and ICRM for the site visit.

The site visit was led by the KACST Director and other distinguished members of the panel on the 25th of April 2010. The CEGMR executed a well drafted plan to run the show. The program started with a welcome address by the Director of CEGMR, Dr. Mohammed Al-Qahtani, followed by a brief overview on the activities of the Center. The Director's lecture was followed by separate discussions between the review panel and the CEGMR teams for CIPM and ICRM. The review panel was greatly impressed with the experience and credentials of the bidding teams. The panel noted, in particular, base investment in the facilities and infrastructure already funded by the CEGMR as one of



the major driving force for the conduct of research proposed in the TIC's. They also noted the research activities highly relevant to Saudi society and the individual researchers proposed as passionate and eager to commit and contribute to the Center-level objectives. The review panel concluded its program by a site tour for the future laboratories of the selected TIC. The Director thanked all the staff for making this historical day a success and wished all good luck in research pursuits.

Based on a stringent set of criteria that included team structure and experience, existing infrastructure, resource deployment plan, importance of the technology and prospects for technology commercialization and the on-site assessment, the KACST finally announced the TIC program award in favor of CIPM in the beginning of October 2010.

The winning proposal aims to establish a new technology innovation center in the field of Personalized Medicine. This center will provide an umbrella under which research into providing tailor-made health care to the people will be conducted and developed. This multi-disciplinary research approach is bound to increase the efficiency of the health care provision to the Saudi society and deliver an overall saving in the expenditure on the health care sector by reducing the cases of mis-diagnosis and side effects caused by wrong drug or dose. The Director of CEGMR, Dr. Al-Qahtani reiterated the fact that the new TIC's were the fruits of the first 5-yearly National Plan for Science and Technology meeting held in 2009 for advancing, supporting and developing the culture of research and innovation in the Kingdom of Saudi Arabia. He further added, "The winning of the CIPM competition is a big success for CEGMR for its long term sustainability and we have to put our team efforts, motivation and social connectedness to enhance its progress."

'Spread the Word': DGMU Approved as Accredited Laboratory





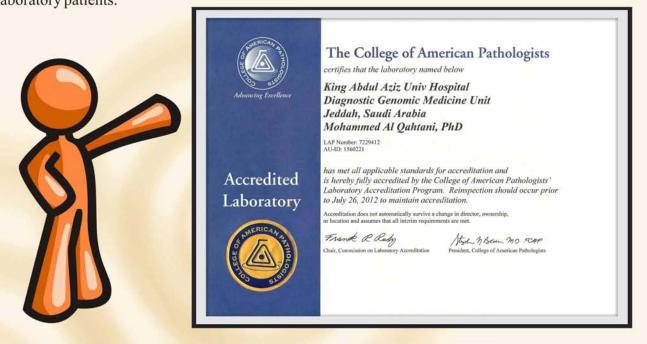
King Abdulaziz University Hospital Diagnostic Genomic Medicine Unit (DGMU), Jeddah, Saudi Arabia, has been awarded accreditation by the Accreditation Committee of the College of American Pathologists (CAP) based on the results of a recent onsite inspection. This was announced to all members of the staff by the Director of CEGMR, Dr. Mohammed Hussein Al-Qahtani on the first day after the Hajj holidays. He added that although the DGMU served as a precursor and a basis for the establishment of the CEGMR, the research at CEGMR will certainly help in providing new ways of diagnosing diseases in addition to improving the already existing services provided by the DGMU.

The CAP Laboratory Accreditation Program is recognized internationally and the only one of its kind that utilizes teams of practicing laboratory professionals as inspectors. During the CAP accreditation process, inspectors examine the laboratory's records and quality control of procedures for the preceding two years. CAP inspectors also examine laboratory staff qualifications as

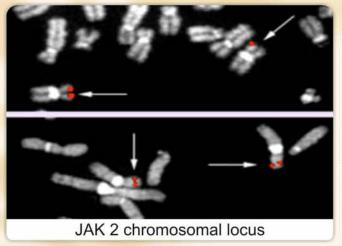




well as the laboratory's equipment, facilities, safety program and record in addition to the overall management of the laboratory. This stringent inspection program is designed to specifically ensure the highest standard of care for all laboratory patients.



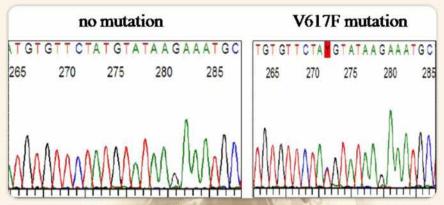
CEGMR Leukemia Research Moves into Diagnostics



Leukemia Research group at CEGMR has found that screening for JAK2 mutations, already recommended by the World Health Organization (WHO) as a major diagnostic and clonal marker in CMPNs worldwide, can also be applied to the patients around Jeddah in the western part of Saudi Arabia. This is a good development at the Center, commented Dr. Al-Qahtani who hopes that the kind of research performed at CEGMR will ultimately help to improve our health care system in the country through advanced scientific knowledge.

The CMPN's are a group of clinically related clonal hematopoietic stem cell disorders in which large numbers of abnormal red blood cells, white blood cells, or platelets grow and spread excess in the bone marrow and the peripheral blood. According to the WHO scheme of classification CMPN'S include chronic myelogenous leukemia [CML, Ph chromosome, t(9;22)(q34;q11), BCR/ABL-positive], chronic neutrophilic leukemia, chronic eosinophilic leukemia (and the hypereosinophilic syndrome), polycythemia vera (PV), chronic idiopathic myelofibrosis (with extramedullary hematopoiesi), essential thrombocythemia (ET), and chronic myeloproliferative disease, unclassified. The mutations in the non-receptor tyrosine kinase JAK2 (JAK2V617F and exon 12) have significantly contributed to our understanding of the molecular mechanisms in the pathogenesis of CMPNs making JAK2 mutations a diagnostic marker to distinguish clonal myeloproliferation from reactive disorders.





The research at CEGMR identified JAK2 mutation (V617F) in around 90-95% of PV patients, obtained with informed consent, from different hospitals around Jeddah. These data are consistent with other published reports from over the globe.

The results of this study are going to be published soon in International

Journal. The Director of CEGMR gave a word of appreciation to the Leukemia team members and wished them success in their research pursuits.

CEGMR Announces Joint Ph. D. Program with an International University

CEGMR is proud to announce the launch of a joint Ph.D program with the University of New Castle. Although started a few years back, it is for the first time that the Ph.D student will work for his/her research at CEGMR with a supervisor form an International University. This was announced during a recent visit to the CEGMR by Professor Jolanta Weaver, a Stem Cell researcher and expert from the University of New Castle. The joint supervision program will help the students to perform their research at CEGMR with all the state-of-the-art facilities while still obtaining their degrees from

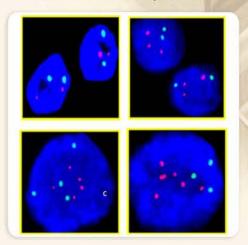


foreign Universities. The program will also enhance international research collaborations with various Universities. These collaborations are vital for the success of our research in the country.

CEGMR's Own Research Findings in Peer Reviewed Journals

Evaluation of HER-2/neu Gene Amplification by Fluorescence in Situ Hybridization and Immunohistochemistry in Saudi Female Breast Cancer.

Al-Khattabi H, Kelany A, Buhmeida A, Al-Maghrabi J, Lari S, Chaudhary A, Gari M, Abuzenadah A, Al-Qahtani M



A team of researchers at CEGMR under the supervision of Dr. Abdelbaset Buhmeida recently reported on the status of HER-2/neu gene amplification in Saudi female breast cancer patients. The authors report HER-2/neu gene and protein over-expression in 25% and 24% of the breast carcinoma cases analyzed respectively with high concordance rate between immunohistochemistry (IHC) and fluorescence in situ hybridization (FISH) techniques both of which are currently being performed at CEGMR and DGMU with great precision and accuracy.

The study published in the scientific journal 'Anticancer Research',



2010 tested the use of IHC and FISH on seventy five effective ductal breast carcinoma samples to evaluate the HER-2/neu gene status and to ascertain the concordance rate between the two methods.

The human epidermal growth factor receptor-2 (HER2) is over-expressed/amplified in a range of solid tumor types including breast, gastric, ovarian, bladder, salivary gland, endometrial, pancreatic and non-small-cell lung cancer (NSCLC). HER2 is implicated in disease initiation and progression, associated with poor prognosis, and may also predict the response to chemotherapy and hormonal therapy. Scientific literature indicates that HER2 status is not only important as a prognostic and predictive factor but signalling through HER2 may lead to the development of novel bio-directed therapies for a wide range of solid tumors.

Despite its value as established prognostic and predictive factor in the Western countries, HER2 status assessment in Saudi patients has not been thoroughly investigated. This study is one step forward in this direction, commented one of the authors who further added that studies on large cohort are required and are underway.

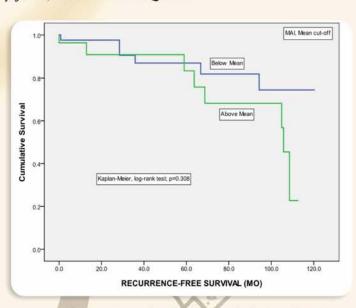
Anticancer Res. 2010 Oct;30(10):4081-8.

Prognostic Value of Mitotic Counts in Breast Cancer of Saudi Arabian Patients

Abdelbaset Buhmeida, Jaudah Al-Maghrabi, Adnan Merdad, Fatima Al-Thubaity, Adeel Chaudhary, Mamdouh Gari, Adel Abuzenadah, Yrjo Collan, Kari Syrjänen, Mohammed Al-Qahtani

A team of researchers from the Breast Cancer group of CEGMR in yet another development reported the prognostic value of mitotic counts in breast cancer of Saudi Arabian patients. The studies due to be published soon were led by Dr. Abdelbaset Buhmeida.

The study involved mitotic count assessment using a standard laboratory microscope in 87 patients treated for breast cancer at the Departments of Surgery and Oncology, King Abdulaziz University Hospital, between 2000-2008. From this study, the authors conclude that the quantitatively measurable mitotic counts of cancer cell nuclei are of significant prognostic value in invasive ductal carcinoma of breast in Saudi Arabia and the mean



cut-off values of mitotic activity index (MAI) and to a lesser extent those of standardized mitotic index (SMI) can be applied as objective criteria to distinguish breast cancer patients into groups with favorable and less favorable prognosis.

CEGMR Outreach Activities

Delegation from Al Mansoura University Visited CEGMR

Dr. Mohammed Hussein Al-Qahtani, CEGMR Executive Director, received a team comprising of Dr. Hassan Abolenein, Director of Urology and Kidney Disease Center, Al Mansoura University, Egypt, and accompanied by Professor. Hesham Moslly, Urology Consultant at King Abdul Aziz University Hospital, Jeddah.



Dr. Ibtessam Hussein Ramzy, a Human Geneticist accompanied the delegation for a short on-site visit to the existing research laboratories and facilities at CEGMR. The visitors were pleased to see the well established laboratories at CEGMR. They wished the Center 'success' in its research pursuits. The visit concluded with the delegation signing in CEGMR visit book followed by photo session.



A Scientific Lecture by Dr. Jolanta Weaver on "Endothelial Progenitor Cells"



Dr. Jolanta Weaver, a specialist in Stem Cell Research in the Institute of Cellular Medicine at New Castle University, UK, presented a lecture titled "Endothelial Progenitor Cells", in the main auditorium of Center of Excellence in Genomic Medicine Research on 3/11/2010, Dr. Weaver talked about endothelial progenitor cells, their isolation, culture and use as a model system to study ischemic hypoxia following cardio vascular arrest. Her lecture is a part of joint PhD program setup between the CEGMR and the international universities. Dr. Weaver will supervise one of the PhD students, Ms Shereen Bakhashab by the collaborative program exchange between the CEGMR and the Newcastle University.

Endothelial cells are the cells that make up the lining of blood vessels. As primitive cells made in the bone marrow, they can enter the bloodstream and go to areas of blood vessel injury to help repair the damage. The number of endothelial progenitor cells in the blood is a risk factor for vascular disease and their depletion may contribute to blood vessel disease. In her lecture, Dr. Weaver also elaborated on the joint research project with CEGMR, wherein she was deeply appreciative of the state-of-the-art facilities like the Affymetrix and Agilent microarray platforms that are vital for the project. The lecture was followed by a series of technical discussions related to the collaboration with the University of New Castle.

CEGMR Lecture Series

A Scientific Lecture by Dr. Ibtessam Hussein Ramzi on the "Genetics of Mental Retardation"

Dr. Ibtessam Hussein Ramzi, a researcher and a geneticist with a PhD in Human Genetics from the Institute of Medical Research, Alexandria University in Egypt presented a scientific lecture on the "Genetics of Mental Retardation" in the CEGMR auditorium on Wednesday 30th June 2010.

Dr. Ramzi in her presentation discussed a number of topics ranging from various causes of mental



retardation, single gene defects and X-linked disorders, microdeletion syndromes, molecular causes and neurobiology of mental retardation. She also elaborated on fragile (FRAX) syndrome, transciptomic and



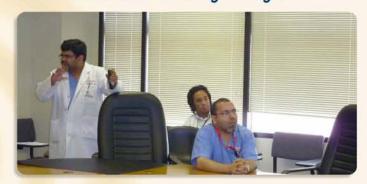


epigenetic studies in mental retardation. She introduced the potential of microarray based comparative genomic hybridization and SNP arrays for the analysis of gain or loss in human genome at the global level.

In her lecture, Dr. Ramzi also talked about her research interests and visions for future research at CEGMR that include aCGH and SNP arrays using the established Affymetrix and Agilent microarray platforms.

A Scientific Lecture by Dr. Sajjad Karim on "Bioinformatics in Drug Design"

Dr. Sajjad Karim, a bioinformatics trained researcher with a PhD in Molecular Biology from Jamia Millia Islamia University, New Delhi, India presented a scientific lecture on the "Bioinformatics in Drug Design" in the CEGMR auditorium on Wednesday 7 July 2010 corresponding to 25 Rajab 1431 H. In his lecture Dr. Sajjad discussed how genomics, proteomics, combinatorial chemistry and



high-throughput screening have all contributed to a massive increase in the amount of data generated by the academia and the industrial sectors. According to him, the vast amount of data generated across disciplines has led to the integration of Bioinformatics and Chemoinformatics, and the development of specialized algorithms. Dr. Sajjad also elaborated on molecular modeling methods, strategies in drug design and protein structure determination. He also gave an overview of the Dell-based 'Bioinformatics-Work Station' and 'Offline Cluster' that are part of the functioning bioinformatics Unit at CEGMR.

Workshops and Training Programs

Applications of PCR in Diagnostic Molecular Genetics



A five-day workshop and training program in molecular cytogenetics was successfully organized between 19.10.2010 and 23.10.2010 at the CEGMR/DGMU attended by a number of students from King Abdulaziz University. The program included theoretical sessions as well as a practical session consisting of 'hands-on' training. The program was coordinated by Mr. Emad Hamzi and other CEGMR researchers. Dr. Adeel G Chaudhary, Deputy Director for Technical Affairs supervised the program.

The topics discussed during the workshop included: recombinant DNA technology, human genome project, PCR overview and PCR primer designing moderated by Dr. Sajjad Karim, various methods of DNA and RNA extraction by Dr. Peer Zada, Gel electrophoresis and RT-PCR by Dr. Farid Ahmed, restriction length polymorphism and its application by Dr. Ashraf, sources of DNA by Dr. Wafa Nichols, and genotyping in relation to disease by Dr. Ibtessam H Ramzi. Mr. Emad, Miss. Wafa, Miss Manar, Mr. Hani Rashad, Miss. Zenab and Miss. Manal Otaibi were involved in practical sessions. All sessions were followed by