Pakistan Journal of Biochemistry and Molecular Biology

Preface

Fourteenth Biennial Conference of Pakistan Society for Biochemistry and Molecular Biology (PSBMB) was held during December 9-12, 2018 at Dr. A.Q. Khan Institute of Biotechnology & Genetic Engineering (KIBGE), University of Karachi, Karachi, Pakistan. Theme of the conference was "MOLECULAR BIOSCIENCES: RESEARCH AND INNOVATIONS". Hundreds of scientists, post-doctoral fellows and graduate students from all over Pakistan and other countries attended this conference.

Here we present abstracts of invited lectures delivered during the conference. Editorial board is grateful to the organizing committee of PSBMB 2018 for providing abstracts of invited lectures for publication in PJBMB.

Editorial board

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Invited Lectures of 14th Biennial Conference of PSBMB (December 2018)

HUMAN GENETIC VARIATIONS AND DISEASES

Abdul Hameed
Institute of Biotechnology & Genetic Engineering (IBGE),
Islamabad, Pakistan

Human genetic variations are the differences in DNA sequence within the genome of individuals in populations and these variations also have many forms. Modern molecular technologies now enable detailed measurements of germline and somatic alterations, many of which underlie human disease. The field of human genetic variations has progressed rapidly over the past few years. It has added much information and deepened our knowledge and understanding of the diversity of genetic variations in the human genome. This significant progress has been driven mainly by the developments of microarray and next generation sequencing technologies. The array-based methods have been widely used for large-scale copy number variations (CNVs) detection in the human genome. The arrival of next generation sequencing technologies, which enabled the completion of several whole genome re-sequencing studies, has also resulted in a massive discovery of novel genetic variations. An enormous amount of human genetic data is now available, and understanding the breadth and complexity of human variation presents one of the greatest scientific challenges of our time. In particular, interpretation of genetic variation and its relevance to disease is critical for the success of

precision medicine programs. Genetic variants can be characterized by their locations in genomic DNA, evolutionary, physico-chemical, structural, and functional properties, their effects on RNA transcripts, proteins, molecular interactions, and ultimately their impacts on human cells and tissues. For many diseases, the molecular mechanisms of pathogenesis have not yet been characterized and innovative methodologies can contribute to future progress. In addition, advances in health informatics, medical genetics, and clinical practice are critical to the translational impact of basic research. By studying genetic variation we hope to understand the molecular process that contributes to life on earth.

MICROBIAL THERAPEUTICS

Aqeel Ahmad
Barrett Hodgson University, Karachi, Pakistan

Microorganisms are generally considered harmful, responsible for causing many diseases. But the beneficial role of microorganisms cannot be denied. For Microbiologist, microorganisms are life sustaining agents, performing diverse activities in nature. Nonetheless, today it is well established that microbes also play protective role in human health.

Microorganisms play pivotal role in the production of novel substances necessary for maintenance of human health. Scientists are trying to link relationships of health and diseases with the presence or absence of microorganisms. The perturbation of normal flora can lead to imbalance and dysbiosis. This has been demonstrated in

inflammatory bowel disease, irritable bowel syndrome, allergy, obesity, colon cancer and even autism. The ability to restore the balance with microbial intervention was also demonstrated.

Probiotics are used to alleviate many diseased conditions. Strains of *Bifidobacterium* and *Lactobacillus* can improve anxiety, depression, autism, obsessive-compulsive disorder (OCD) and memory. Some probiotics may help protect the heart by reducing "bad" LDL cholesterol levels and modestly lowering blood pressure; may reduce the risk and severity of certain allergies, such as eczema in infants; *E. coli Nissle* was just as effective as drugs in maintaining remission in people with ulcerative colitis; may help boost immune system and protect against infections.

The human microbiota consists of the 10-100 trillion symbiotic microbial cells harbored by a man, which is 10-100 time higher than the total human cells present in a body; while the human microbiome consists of the genes these microbes harbor. Gut microbes are considered a major source of important mediator for maintaining life. Many laboratories are now engaged in analyzing the type, number and potentials of microbes found in gut. However, due to difficulty in culturing and identification of microbes, scientists are trying to determine the microbiome sequence. Any deviation from normal are being studied for health or diseased condition. If these microbes or their genome sequences, in gut, are analyzed and their relationship with health and disease are established, then various genetically modified species can be developed and used as medicine in future.

The therapeutic microbes can be applied in human and veterinary medicine. Possible indications include

vaccination, immunomodulation, inflammation, cancer, infectious diseases and metabolic disorders. Microbes can be administered orally, intranasally or intrapulmonary. The therapeutic use of microbes has a bright future, as can be deduced from exciting findings of microbiota studies that are reported daily, as well as numerous successful proof-of-principle reports from animal models. The overall advancement of the challenging field is the main goal.

Emerging technologies such as fecal transplantation, whole-genome sequencing, maintaining human microbial communities in experimental animals, and the creation of gene manipulated culture collections for treatments of different diseases. The knowledge of balanced microbiota, microbial physiology and human pathophysiology can lead to identification of the microbial strain/s or mixtures, or improving existing microbial strains by mutagenesis, genetic manipulation and synthetic biology. The new species will exceed the existent probiotic definition and food applications but may well be adopted by the pharmaceutical industry.

Pharmacy is the science and technique of preparing and dispensing drugs with the aim to ensure the safe and effective use of pharmaceutical products. Microbial pharmacy may include the use of microbes for health benefits and their preparation as pharmaceutical products in the form of tablets, capsules or powders, containing bacteria in dried form, can help establishing new branch of MICROBIAL THERAPEUTICS.

DIFFERENTIATION OF RAT BONE MARROW MESENCHYMAL STEM CELLS INTO CARDIOMYOCYTES: ROLE OF SMALL MOLECULES

Asmat Salim, Irfan Khan, Nadia Naeem, Anwar Ali and Kanwal Haneef
Dr. Panjwani Center for Molecular Medicine and Drug Research, International Center for Chemical and Biological Sciences, University of Karachi, Karachi-75270, Pakistan

Cardiovascular diseases (CVDs) are the number one cause of death globally. Current therapeutic approaches are limited in preventing ventricular remodeling following myocardial infarction (MI). Therefore, novel therapeutic approach of transplantation of exogenously differentiated cardiomyocytes could be a better option. Mesenchymal stem cells (MSCs) have been used for the treatment of MI to repair the injured myocardium and improve cardiac function. However, donor cells have limited capacity to differentiate into functional cardiomyocytes in the ischemic microenvironment of the heart. Among other strategies, small molecules have been identified that promote differentiation of MSCs into functionally active cardiac-like cells. The treated or pre-conditioned stem cells generally show better cell survival, increased differentiation, enhanced paracrine effect, and improved homing to the injury site by regulating the expression of tissue-protective cytokines and growth factors. Pre-conditioning has also shown promising results with respect to cardio-protection as it stimulates endogenous mechanisms resulting in multiple cellular responses. Some examples include 2, 4 dinitrophenol (DNP), 5-azacytidine and its analogues etc. Other synthetic and naturally

occurring compounds have also been tested and were found to be good candidates for future cell-based therapeutics against cardiovascular diseases. Our studies using small molecules for cardiac regeneration resulted in the better fusion, cell adhesion, and differentiation of cardiac markers. Our *in vivo* studies have also shown significant reduction in scar formation, maintenance of left ventricular wall thickness, and increased angiogenesis as revealed by histological analysis and echocardiography. In this presentation, potential role of small molecules on the cardiac differentiation of MSCs will be highlighted.

METAGENOMIC EVALUATION REVEALS DOMINANCE OF ACIDOGENIC BACTERIOME IN SALIVA OF TYPE 2 DIABETIC PATIENTS

M. Kamran Azim[2], Junaid Ahmed Kori[1], Faizan Saleem[1,2] and Arshad Hasan[3]

[1]International Center for Chemical and Biological Sciences, University of Karachi, Karachi-75270, Pakistan

[2]Department of Biosciences, Mohammad Ali Jinnah University, Karachi, Pakistan

[3]Dow Dental College, Dow University of Health Sciences, Karachi, Pakistan

Diabetes mellitus is characterized as one of the most prevalent and complicated metabolic disorders around the globe. It has been proposed that oral microbial flora varies in response to the diabetes. In this study, we have carried out 16S rRNA metagenomic characterization of oral microbial communities in diabetic patients (n=49) in comparison to healthy individuals (n=55) to confer upon the variations in Pakistani population. We observed that

among the bacterial phyla *Bacteroidetes* and *Firmicutes* predominated in diabetics in comparison to healthy individuals. On the genus level, several bacterial genera were found to be either exclusive or in higher abundance in saliva of diabetics among which the acidogenic bacterial genera i.e. *Prevotella*, *Veillonella* and *Laptotrichia* were dominant. This observation suggested involvement of these eubacteria in dental caries in diabetics. PCA analysis demonstrated significant microflora differences in diabetic females and male. The present study provided additional information related to oral microbial communities in type 2 diabetes.

NANOMEDICINE: AN INTERDISCIPLINARY PLAY TO COMBAT THE DISEASES

Muhammad Ismail
Institute of Biomedical & Genetic Engineering (IBGE),
24 Mauve Area, Sector G-9/1, Islamabad, Pakistan

Interdisciplinary research has revolutionized the field of medicine and we have witnessed exponential increase in the high-impact research in past few decades. Rapidly developing resistance, modest clinical outcome and off-target effects are some of the major stumbling blocks which have confounded standardization of therapy. Medicinal chemistry and nanotechnology may have the answers to outstanding questions of clinicians and can prove to be efficient in successful translation of therapeutics from bench-top to the bedside. Excitingly, many bioactive ingredients isolated from natural sources having experimentally proven efficacy are currently being tested for improved bioavailability by

conjugation with different nanoparticles or by using different nanotechnologically assisted delivery systems.

Our group has worked on silver nanoparticles synthesized through microalgae demonstrated considerable anticancer, anti-bacterial and antiviral activity. We also tested different plants for biological activities. *Cassia angustifolia* was noted to be an effective against different cancer cell lines and microbes. Structures of the bioactive compounds isolated from *Cassia angustifolia* were elucidated by NMR and ESI-MS spectrometry. *Pine roxburgii* and *Ricinus communis* were effective against multi-drug resistant *Klebsiella pneumonae*. Moreover, biological applications of Ce doped CuO nanoparticles, Cu and Mg Doped ZnO Nanoparticles alone or in conjugation with extract from medicinal plants. We have reported significant antibacterial activity displayed by these conjugates. We also provide evidence of targeted killing of Multi-drug Resistant Bacteria by Ni Doped ZnO Nanorods and Ag doped ZnO nanorods. Recently, we have experimentally verified that Sn doping induced enhancement in the activity of ZnO nanostructures against antibiotic resistant S. aureus bacteria. Future studies must converge on a better and considerably improved understanding of the healing effect and toxicological profiling of the nanotechnologically delivered drugs in animal models.

BRIEF HISTORY OF MICROBIOLOGY AND LABORATORY ACQUIRED INFECTION

Shahida Mumtaz Qureshi
Paeds Infectious Disease Research Lab,
Aga Khan University, Karachi, Pakistan

The history of microbiology gained recognition from 1857 when the modern Disciplines such as Bacteriology, Protozoology Mycology, Parasitology were studied in depth by the Known scientists The Golden era of Microbiology was during the period of 1857-1907 when famous Scientist such as Koch, Pasture, Buchner etc stirred marked discoveries in Industrial Microbiology, food and Beverage Technology, Microbial Metabolism, Microbial Genetics and Genetic Engineering, Virulence and Etiology of Infection was studied in detail by Koch.

Intensive work in Lab brought about the occurrence of Laboratory Acquired Infection (LAI):

The link between LAIs and Biosafety is obvious. These concerns are also to be considered as one of the underlying reasons for the elaboration of containment measures and application of safe work practices.

LAIs are defined as: All infection acquired through laboratory or laboratory-related activities regardless whether they are symptomatic or asymptomatic in nature.

Safe Laboratory practices will have to be implemented to reduce the LAI, Training of Laboratory staff to proper Biosafety practices and Proper documentation of Incidence is Mandatory to minimize Laboratory Acquired Infections.

THE *BACILLUS CEREUS* GROUP: AN EXCEPTIONAL RESERVOIR OF BIOACTIVE SUBSTANCES

Shakeel Ahmed Khan
Department of Biosciences, Barrett Hodgson University,
Karachi, Pakistan

The overall ecological balance on this planet is maintained by associations between various life forms, in one way or another. Alongside the plants, the importance of microorganisms cannot be ignored in maintaining the energy pyramid. For ages, microorganisms have been associated with soil as decomposers. They are the common inhabitant of rhizosphere and thus aid plants by producing plant growth-promoting substances such as gibberellins. They play a key role in the production of useful food products such as yogurt, cheese, wine, pickles etc. Furthermore, their metabolic products such as enzymes, toxins, antibiotics and surfactants are applicable to medicine, laundry, beverages and food-processing industries. On the contrary, they can be a nuisance if associated with a disease, corrosion or deterioration of materials.

Bacteria belonging to genus *Bacillus* have gained interest due to their ability to produce a large array of useful metabolic products during different stages of their life-cycle. Most of the species can grow on simpler nutritional substances and are capable of surviving under a wide range of physiological. Thus, this tendency of physiological diversity was coined for decades with the acquisition of novel and applicable products of industrial interest.

The importance of most of the strains of *B. cereus* group from economical, medical and biodefence point of view made it a model for genomic studies. This is the most thoroughly studied group of genus *Bacillus* for comparative genome analysis with closely related fully sequenced genomes. In this presentation, the importance *B. cereus* group will be discussed.