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Selected Abstracts from GENOPRO-2017- 4th International Conference on

"Emerging Trends in Protein Science and Proteomics"

(Sponsored by DST-SERB and ICMR, New Delhi and Invertis University, Bareilly)

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ORGANIZED BY DEPARTMENT OF BIOTECHNOLOGY, INVERTIS UNIVERSITY, BAREILLY

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Dr. Nitesh Poddar

Co-convener:
Dr. Dinesh Kumar

Organizing Secretary
Er. Sachin Srivastava

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GENOPRO-2017 INTERNATIONAL CONFERENCE SUMMARY

The Department of Biotechnology (**Convener: Dr. Nitesh Poddar**, Co-convener: Dr. Dinesh Kumar; Organizing Secretary: Er. Sachin Srivastava) organized the 4th International conference entitled **"Emerging trends in protein science and proteomics: GenoPro2017" on 15th and 16th Sep, 2017.** The theme of the conference is to understand the structural–functional relationship of each protein contents in the whole proteome with the help of cutting edge proteomics tools. Protein science is a cross-disciplinary nomenclature encompassing segments of scientific fields such as molecular biology, biochemistry, proteomics, genetics, bioengineering and nanotechnology. The GenoPro2017 international Conference was sponsored by DST-SERB, ICMR, New Delhi and Invertis University, Bareilly.

In this 4th international conference GenoPro2017, **Dr. Shashi Bala Singh**, DS & Director General-Life Sciences (LS), DRDO, New Delhi graced and honored as a Chief Guest. She talked about the biomarkers used in protein science and new fields of proteomics such as nutritional proteomics and translational proteomics.

Prof. Yaakov (Koby) Levy, Department of Structural Biology, Weizmann Institute of Science Rehovot, Israel was Keynote Speaker in GenoPro2017. He talked about the molecular principles such hopping and sliding mechanism for optimizing protein-DNA interactions in many regulation process involved in living system.

Prof. T. P. Singh, Senior Scientist, INSA Senior Scientist, AIIMS, **Prof. Faizan Ahmad,** INSA Fellow, JMI, New Delhi and **Prof. I. D. Mall**, Distinguished Prof., IIT Roorkee were honored as Guest of Honors in GenoPro2017.

Some other eminent scientist such as **Dr. Maansa Raghavan**, Cambridge Univeristy, UK; **Dr. Kakoli Bose**, ATREC, Mumbai; **Dr. Yogendra Sharma**, CCMB, Hyderabad and many more scientists had come all the way from different parts of the country and delivered interesting talks in GenoPro2017.

There were more than 400 research scholars, faculties and student from different parts of India and took active participation in different sessions like: Poster, Oral, Young Scientist and Nobel Research for GenoPro2017 international conference. This conference enlightened various young and innovative minds about the different perspectives of protein science & proteomics. Thus the International conference-GenoPro2017 had made a grand success and achieved a milestone in the field of Protein Science and Proteomics

The conference was warmed by the presence of **Honorable Chancellor Dr. Umesh Gautam** and Chief Guest **Dr. Shashi Bala Singh**, Director General -Life Science, Defense Research and Development Organization, New Delhi. **Dr. Umesh Gautam** has given a warm welcome to eminent scientists / Professors, beside that he announced that we will be collaborate Centre for Cellular and Molecular Biology (CCMB), Hyderabad. After that welcome address was conveyed by **Dr. Jagdish Rai**, Vice Chancellor, who welcomed Chief Guest and Invited Speakers. **Mr. L. P. Mishra** (Retd. IG, UP Police), Director Administration has given his speech in which he talked about Ethics and moral values of human being. He also enlightens the audience by giving a brief note on how Indian society, Vedas and science are co-related. After that the podium was handed over to **Dr. R. K. Shukla**, Dean Engg. and Science. He has delivered a short note on the eve of Engineers Day and has given tribute to greatest Indian Engineer Bharat Ratna **Dr. Mokshagundam Visvesvaraya** (popularly known as Sir MV). In spite of that he enlightens the young and innovative minds to follow leader like him. He also shows gratitude to the Department of Biotechnology and his blessing to the **Dr. Ravi Deval (HOD),** organizing committee and all the faculty of department. Special thanks were given to **Dr. Nitesh Kumar Poddar (Convener), Dr. Dinesh Prajapati (Co-Convener)** and **Mr. Sachin K. Srivastava (Organizing Secretary)** for the brilliant effort laid by them.

Strategies to Restore Function to Disease Causing Missense Mutant Proteins

Singh L. R.
Dr. B. R. Ambedkar Center for Biomedical Research, University of Delhi, INDIA.
E-mail: lairksingh@gmail.com

ABSTRACT

Missense mutant proteins, such as those produced in individuals with genetic diseases, are often misfolded and subject to processing by intracellular quality control systems. Previously, we have shown using a yeast system that enzymatic function could be restored to I278T cystathionine beta-synthase (CBS), a cause of homocystinuria, by treatments that affect the intracellular chaperone environment. Here, we extend these studies and show that it is possible to restore significant levels of enzyme activity to 17 of 18 (94%) disease causing missense mutations in human cystathionine beta-synthase (CBS) expressed in Saccharomyces cerevisiae by exposure to ethanol, proteasome inhibitors, or deletion of the Hsp26 small heat shock protein. All three of these treatments induce Hsp70, which is necessary but not sufficient for rescue. In addition to CBS, these same treatments can rescue disease-causing mutations in human p53 and the methylene tetrahydrofolate reductase gene. These findings do not appear restricted to S. cerevisiae, as proteasome inhibitors can restore significant CBS enzymatic activity to CBS alleles expressed in fibroblasts derived from homocystinuric patients and in a mouse model for homocystinuria that expresses human I278T CBS. These findings suggest that proteasome inhibitors and other Hsp70 inducing agents may be useful in the treatment of a variety of genetic diseases caused by missense mutations.

Mechanism of Survival of Ethanol Producing Organisms: Role of Cellular Compatible Osmolytes in Counteracting the Deleterious Effects of Ethanol on Structure, Stability and Function of Proteins

Ilyas Beg, Asimul Islam, Md. Imtaiyaz Hassan and Faizan Ahmad
Centre for Interdisciplinary Research in Basic Sciences, Jamia Millia Islamia, Jamia Nagar, New Delhi 110025, INDIA.
E-mail: fahmad@jmi.ac.in

ABSTRACT

Saccharomyces cerevisiae, a unicellular eukaryote, is one of the most extensively studied organisms for its ethanol tolerance capabilities. It is observed that *S. cerevisiae* accumulates and tolerate up to 19.8% (w/v) ethanol during the process of fermentations, whereas other organisms die at this high ethanol concentration due to denaturation of their plasma membrane and cellular enzymes. We asked a question: How does *S. cerevisiae* tolerate the deleterious effects of ethanol and maintain its cellular integrity in the presence of high ethanol concentrations? It has been reported that *S. cerevisiae* undergoes various metabolic changes, and the accumulation of trehalose, glycerol and proline (compatible osmolytes), is one major and an important factor observed during ethanol production. It is known that these compatible osmolytes increase the cell viability and maintain the cellular integrity of *S. cerevisiae* during ethanol stress. What is not known whether these osmolytes counteract the deleterious effects of ethanol on the structure, function and stability of cellular proteins during ethanol stress. To determine the efficacy of each osmolyte to counteract the deleterious effects of ethanol on thermodynamic stability of proteins, we have measured thermal denaturation of lysozyme, apo α–lactalbumin, and yeast iso–1–cytochrome *c* in the presence of multiple concentrations of individual osmolyte and ethanol alone and in combination at different pH values by following changes in molar absorbance coefficient ($\Delta\varepsilon_\lambda$) at different pH values. Each thermal denaturation curve (plot of $\Delta\varepsilon_\lambda$ versus T) was analyzed for T_m (midpoint of denaturation) and ΔH_{em} (enthalpy change at T_m) through non–linear fit. The slop of the plot of ΔH_m versus T_m, yielded ΔC_p (constant-pressure heat capacity change). Values of T_m, ΔH_m and ΔC_p were then used to estimate ΔG_D° (standard Gibbs free energy change at 25 °C). It has been observed that thermodynamic stability of each protein increases with increasing concentrations of each osmolyte whereas opposite effect is true for ethanol. These observations can be explained by the theory developed earlier.[1,2] Functional activity of lysozyme was also measured in the presence of each osmolyte and ethanol alone and in the combined mixture of osmolyte and ethanol. Main conclusions of our study are: (a) trehalose and proline have the ability to counteract the deleterious effects of ethanol on stability and functional activity of proteins, (b) glycerol loses its stabilizing ability in the presence of ethanol, and (c) on the molar scale trehalose is a better counteracting agent.

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The 'ancient biomolecular revolution' and the reconstruction of our evolutionary past

Maanasa Raghavan
Cambridge University, UK.

ABSTRACT

While biology, in general, has benefited immensely from the '-omics' revolution, the sub-field of ancient biomolecules – the study of DNA (genomics), RNA (transcriptomics) and proteins (proteomics) from ancient specimen – has also been gaining a steady foothold within evolutionary biology. The analysis of ancient biomolecules has the potential to provide direct insights into the population histories of various species and gain an understanding of the mechanisms and rates of evolutionary changes, while circumventing the need for assumptions and extrapolations based on data from present-day samples. In this talk, I will provide examples of how molecular studies are increasingly making use of ancient specimen to unravel evolutionary trajectories of both extinct and extant species. Such studies are valuable in their contribution to several fields including conservation science, population genetics as well as medical genetics.

Therapeutic Targeting of Human Kinases to Control Cancer Progression: An alternative Approach

Md. Imtaiyaz Hassan
Centre for Interdisciplinary Research in Basic Sciences, Jamia Millia Islamia, Jamia Nagar, NEW DELHI - 110 025, India
E-mail: mihassan@jmi.ac.in

ABSTRACT

Human kinases are important drug target for cancer and neurodegenerative dieseases. In this study, we have evaluated different natural dietary polyphenolics including rutin, quercetin, ferulic acid, beta carotene, hesperidin, gallic acid and vanillin as inhibitor of human kinase especially Microtubule Affinity Regulating Kinase 4 (MARK4) and Human calcium/calmodulin-dependent protein kinase IV (CAMKIV). All compounds are primarily binds to the active site cavity and inhibit their enzyme activity at a considerable extent. Molecular docking was further complemented by the fluorescence-binding studies and isothermal titration calorimetry (ITC) measurements. We found that rutin and vanillin bind to MARK4 and CAMK4 with a reasonably high affinity. ATPase and tau-phosphorylation assay further suggesting that rutin and vanillin inhibit the enzyme activity of both kinases at a great extent. Cell proliferation, ROS quantification and Annexin-V staining studies are clearly providing sufficient evidences for the apoptotic potential of rutin and vanillin. In conclusion, rutin and vanillin may be considered as potential kinase inhibitors and further exploited to design novel therapeutic molecules against associated diseases.

Structural basis of antibacterial action of innate immune proteins and their applications as Protein-Antibiotics

T.P. Singh
Department of Biophysics, All India Institute of Medical Sciences, New Delhi

ABSTRACT

Considering the alarming rise in the incidence of bacterial resistance to known antibiotics, there is a desperate need to develop bacterial resistance-free antibiotics. The proteins of the innate immune system provide the first line of defense against infecting microbes. These proteins recognize the conserved motifs that are present on the cell walls of bacteria. Thus the success of the innate immune system depends on the affinity of the proteins of innate immune system towards the bacterial cell wall molecules. The conserved motifs of microbial cell walls

are called pathogen associated molecular patterns (PAMPs) that include the well known peptidoglycans (PGN) and lipopolysaccharides (LPS) of Gram-negative bacteria, PGN and lipoteichoic acid (LTA) of the Gram-positive bacteria and mycolic acid (MA) and other fatty acids of *Mycobacterium tuberculosis*. These PAMPs are classified into two groups: (i) those which contain glycan moieties such PGN, LPS, LTA etc. and (ii) those that are derivatives of fatty acids such as MA. Therefore, there should be two independent binding sites for the two different types of PAMPs. The PAMPs are specifically recognized by innate immunity molecules which are historically known as peptidoglycan recognition proteins (PGRPs).These proteins bind to PAMPs with significant affinities and neutralize the infecting pathogens through a variety of actions. There are four types of PGRPs in mammals including humans, PGRP-L (MW = 90kDa), PGRP-Iα and Iβ (MW = 45kDa) and PGRP-S (MW = 21kDa). PGRP-S represents the domain that has the binding site for PAMPs. The binding affinities of PGRP-S and structures of unbound and bound PGRP-S from various species showed that the protein from camel has considerably higher affinity than those of other animals including humans. The epidemiological data indicate that the camels have the lowest rates of infections. Structurally, PGRP-S from camel exists in the form of a dimer whereas the human protein acts as a monomer. There are only a few sequence differences in the proteins from two species which are responsible for dimerization of camel protein. As a result of dimerization, a deep binding cleft is formed in the camel protein whereas only a shallow cleft is present in the case of human monomeric protein. Because of dimerization, the potency of camel protein is much higher than the same protein from other species. Thus if camel protein is used or a suitably mutated human protein is prepared and used, the fight against bacterial infection will improve.

The mechanism of action of PGRP-S involves an effective sequestration of bacteria which results in the killing of bacteria. Since PGRP-S interacts with bacterial cell wall, the kinetics of bacterial cell death appears to be similar to those antibiotics which inhibit the biosynthesis of PGN. Due to this similarity, PGRP-S is suggested to be termed as **"protein antibiotics"** and since they bind to bacterial cell wall molecules the issues of side effects and resistance will not arise and if the potencies are high, the invading bacteria can be tackled rapidly.

Biotechnology Application in Pulp and Paper Industry and Protein Recovery from Paper Mill Waste

Prof. I. D. Mall

Former Professor & Head Dept. of Chemical Engg. IIT Roorkee, Former Distingushed Professor and Head Chemical engg. University of Petroleum and Energy Studies(UPES) Dehradun

ABSTRACT

There are about 6.5 billion people living on planet Earth. Worldwide paper consumption in this century has increased 4 times faster than population. Paper and paperboard worldwide will reach 400 million tones in 2011 and 640 million tones in 2020 with world population of 8000 million people and per capita consumption of paper and paperboard of 80 kg. There are about 500 Kraft mills and many thousands of other types of pulp and paper mills in the world. Though India's per capita consumption is quite low as compared to world average, it is estimated that paper demand in India is estimated 20 million tonnes by 2020 .

Biotechnology has aroused wide interest worldwide due to its diverse applications. It has gained promising position in pulp and paper industry. Some of the major are where biotechnology is has gained promising position are

- Forest management for boosting productivity
- Biodebarking
- Bio pulping :Bio chemical and Biomechanical (fungal pretreatment of wood)
- Enzymatic Pith Removal
- Enzymatic bleaching, for removal of colour and toxic compounds like chlorinated phenols
- Bio deinking
- Improving Pulp drainage
- Aerobic treatment of wastewater:Land application and irrigation,Activated sludge, trickling filter and rotatin biological disc system
- Aqua culture treatment of wastewater
- Anaerobic digestion of Sludge for energy recovery
- Biorefinery concept for biomass: Sustainable bioprocessing of biomass for production of alcohol and alcohol based chemical
- Corrosion control
- Utilisation of spent sulphite liquor for single cell proteinprotein
- Protein recovery from sludge for single cell protein , adhesive
- Protein rich animal feed

Crude protein production from the solid waste residues is comparable to that obtainable from other sources. Some of these waste residues, especially the Kraft pulp mill rejects, appear to be promising sources of substrate for single-cell protein production

Biotechnology has played promising role in paper industry and being used extensively in bio[puling, biobleaching, bio deinking bio energy generation, protein recovery from paper industry waste

Mechanism of DISC Formation-a Prerequisite for Initiation of Extrinsic Cell Death Pathway

Kakoli Bose
ACTREC, Tata Memorial Centre, Kharghar, Navi Mumbai-410210, INDIA
Email: kbose@actrec.gov.in

ABSTRACT

Apoptosis or programmed cell death is a key phenomenon in multicellular organisms that are essential for embryonic development, cellular homeostasis, and immune regulation. Imbalance in this tightly controlled process results in severe pathologic conditions, such as cancer, autoimmune diseases, and neurodegenerative disorders. Classical apoptotic cascades follow two distinct pathways: the intrinsic pathway, which originates in the mitochondria, and the extrinsic pathway, which is triggered by ligation of cell-surface death receptors, followed by formation of a multiprotein death-inducing signaling complex (DISC). The caspases, a family of cysteinyl proteases that initiate and execute apoptosis, rely on these events for their activation and subsequent proteolytic functions. In the Fas-receptor-mediated extrinsic cell death pathway, activation of the initiator caspase-8 is achieved through interaction of its pro-form (procaspase-8) with an adapter protein, Fas-associated death domain (FADD). This interaction is mediated via their similar death effector domains (DEDs) leading to a functional DISC formation and subsequent activation. Although much progress has been made in decoding the major players in this pathway, the structural overview of DISC is still elusive, mainly because of its complicated interaction networks and lack of information on DED proteins. Dissecting the precise mode and the binding interface of DED–DED interaction network holds the key to identifying the missing links in deciphering the unknown steps in DISC formation and subsequent cell death. Here, we provide an intriguing insight into the molecular basis of DED chain formation and define the surface for the physical interaction between FADD and procaspase-8 using interdisciplinary tools. Based on the detailed analyses of the interface for DED–DED interactions, together with data on the FADD–procaspase-8 complex, we propose a new model for DISC formation, regulated at the level of DED-containing proteins.

Molecular principles for optimizing protein-DNA interactions

Yaakov (Koby) Levy
Department of Structural Biology, Weizmann Institute of Science, Rehovot, Israel, 76100
Koby.Levy@weizmann.ac.il

ABSTRACT

Interactions between proteins and nucleic acids are ubiquitous and central to the life of cells. The remarkable efficiency and specificity of protein-DNA recognition presents a major theoretical puzzle given the size of the genome, the large number of molecular species *in vivo* at a given time, and the crowded environment they inhabit. The fast association between proteins and DNA is governed by nonspecific interactions that allow protein sliding along DNA where the protein binds DNA nonspecifically and performs a helical motion when it is placed in the major groove. We have explored using various computational approaches the interplay between the molecular characteristics of the proteins (e.g., DNA recognition motifs, degree of flexibility, and oligomeric states) and the nature of sliding, intersegment transfer events and the overall efficiency of the DNA search. Another important aspect of the search is how the in-vivo conditions (for example, crowding in the cell or coverage of DNA by nucleosomes) affect the efficiency of DNA search. Protein sliding may occur on single-stranded DNA as well, yet via a different mechanism than that for double-stranded DNA. Furthermore, the interaction between proteins and DNA also has to result with high affinity complexes. In my presentation, I will discuss the molecular features of proteins and of the nucleic acids that allow fast dynamics and high affinity binding on both single- and double-stranded DNA.

Genomics Advances And Its Inferences In Understanding The Human Population History

Niraj Rai
Birbal Sahni Institute of Palaeosciences, Lucknow

ABSTRACT

The field of human population genetics has progressed rapidly over the past two decades. It has added impressive information and expanded our knowledge and understanding of the diversity of genetic variations in the human genome. This significant progress has been driven mainly by the advancement of DNA sequencing and genotyping technologies. The aim of my talk is to summarize the latest developments in the field of genetic studies in India and establishing a plausible and well-supported outline for South Asian demographic prehistory. I will present extensive high-coverage sequencing data and its interpretation on targeted modern and ancient samples, autosomal SNP genotyping of specific populations, extensive Y chromosomal genotyping results in the context of human genomic variation worldwide. Finally, I will also discuss the future directions in the field of human population genomics and their impacts on our society.

Calcium signaling via diverse Calcium-binding proteins

Yogendra Sharma
CSIR-Centre for Cellular and Molecular Biology (CCMB), Hyderabad

ABSTRACT

Calcium is not only an essential structural component as an important cation, but also a 'signal of life and death' that controls numerous cellular processes such as cell division and growth, secretion, ion transport and muscle contraction. Through temporal and spatial changes of calcium concentrations and by binding proteins with different affinities, calcium ions mediate calcium TRAC-dependent functions by inducing conformational changes, stabilizing their target proteins, protecting from degradation, and regulating domain interactions. For example, neuronal calcium sensor-1, an intracellular EF-hand calcium-binding protein, regulates several processes in myristoylation and calcium-dependent manner. My laboratory focuses on understanding the process of calcium signaling via such calcium-binding proteins. These calcium-binding proteins are defined based on the structural motifs at which Ca2+ binds. Three Ca2+-binding motifs are (i) the EF-hand motif: we have been working on several related and unrelated proteins of this family (such as neuronal calcium sensor-1, neurocalcin, VILIP, caldendrin, calneurons and secretagogin). We focus on understanding the degenerate motifs, myristoylation signaling, and roles of these proteins in synaptic plasticity. (ii) beta gamma-crystallin type Greek key motif: during the past few years, we have identified a novel calcium-binding motif in the proteins of the βγ-crystallin superfamily. The βγ-crystallin superfamily comprises diverse members from various taxa, ranging from microbes and vertebrates. Our hypothesis is recently proved that many members of the superfamily are Ca2+-binding proteins. These are the members, which contains the canonical motif of ion binding. We are yet to identify the involvement of calcium ions in dictating the functions of these proteins.

Stabilization of Proteins: Volume Exclusion Versus Soft Interactions

Asimul Islam*, Ph.D.
Centre for Interdisciplinary Research in Basic Sciences, Jamia Millia Islamia, Jamia Nagar, New Delhi 110025, India.

ABSTRACT

A sword with double-edge (Volume Exclusion Versus Soft Interactions), effect of macromolecular crowding on protein stability and folding is being ambiguous with recent research. It is showing assorted results of having both stabilizing and destabilizing effects. Organisms acclimate in extreme stress conditions by accumulating small molecules called osmolytes, which induces stabilization in proteins by molecular crowding. We investigated the role of sugar osmolytes on structure, function and stability of proteins. The excluded volume of osmolytes varied with shape and size of osmolyte. Most of the studies to understand protein folding have been done in dilute solutions. However, the cellular environment is crowded with macromolecules of different sizes, shapes and compositions, such as DNA, RNA, proteins, ribosomes and cytoskeletal elements. To understand the consequences of such crowded environment, we investigated the effect of macromolecular crowding on the stability and activity of hen egg white lysozyme, a-lactalbumin and ribonuclease A. The results indicate that owing to volume exclusion, proteins are stabilized, however, the stabilization of the protein is more at lower pH where the effect of exclusion is more. Most of the

studies have demonstrated that volume exclusion plays major role in crowded environment, however, we also investigated the role of soft interactions, in the case of myoglobin. The tertiary structure of myoglobin was perturbed in the presence of polyethylene glycol and ficoll 70, whereas, the secondary structural content remained constant. It was observed that polyethylene glycol and ficol 70 induces molten globule state in myoglobin. Moreover, ITC showed strong binding between myoglobin and PEG, and myoglobin with ficoll 70 at the physiological pH. ITC results indicate that the reason behind this unique behavior of ficoll 70 towards myoglobin may be interaction of ficoll 70 with the heme group of myoglobin. We hypothesize that the soft interactions between heme and ficoll 70 leads to the formation of molten globule conformation myoglobin under physiological conditions. We caution that the binding of protein with crowder and other soft interactions need to be gravely well thought-out when studying macromolecular crowding.

*Author to whom correspondence should be addressed. Phone: +91-9312812007. E-mail: aislam@jmi.ac

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Function Prediction using Association Based Transformation of Protein Interaction Networks.

Kumari, Aparna[1(a)]; Roy, Biswajit[1(b)]

[1]Information Technology Group and Bioinformatics Centre, CSIR-Centre for Cellular and Molecular Biology, Hyderabad, India

[(a)] First Author; [(b)] Presenter

ABSTRACT

Protein-Protein Interaction (PPI) networks are one of the most important types of biological information which has been often and predominantly studied for the discovery of various biochemical mechanisms, identifying different functional modules as well as prediction of individual protein functions. Protein-Protein Interactions (PPI) has been considered as one of the basic elements for most of the biological processes that are taking place within cells. Advances in high throughput PPI screening techniques have enabled the decoding of binary interactions and led towards explaining substantial parts of the entire protein interaction set for several species. Thus, large-scale interaction maps of single organisms are build as well as various cross-species interactions has been established. These large datasets of interactions can be easily represented in the form of networks, where the nodes represent proteins and edges represent interactions. But the conventional techniques to analyze these data can be expensive and time consuming. Hence, in this research the PPI networks are represented using graphs so that effective utilization of data mining techniques for studying association and predicting functions can be accomplished.

However, it is well known that these networks are often both incomplete and inaccurate, i.e., they may have edges which are graph wise invalid, but at the same time often the biologically valid edges remain missing. One way to handle this issue is by transforming the original interaction graph into new graphs that remove invalid edges, add biologically valid ones, and assign reliability scores to the edges constituting the final network. Our study applies association-analysis based data mining techniques for graph-transformation iteratively. Thus an optimized derived network is achieved for better function prediction which is based on the statistical concept of h-confidence. Finally, our investigation highlights an improved function prediction method for proteins having unknown functions as well as deciphering unknown functions of known proteins.

Keywords : Protein-Protein Interaction (PPI) Networks; Protein function prediction; Graph transformation; Data Mining; h-confidence.

Identification of cellular proteins as novel drug targets in Candida glabrata

Navin Kumar[1#] Payal Gupta[1], Ramesh C. Meena[2]

1Department of Biotechnology, Graphic Era University, Dehradun-248002, Uttarakhand

2 Defence Institutes of Physiology and Allied Sciences, Lucknow Road, Timarpur, Delhi-54

Corresponding Author: Navin Kumar, PhD, Associate Professor, Department of Biotechnology, Graphic Era University, Dehradun -248002

Contact No. +91-7417325585; E. Mail: navinbajpai@gmail.com; navinkumar.bt@geu.ac.in

ABSTRACT

Candida is a fungal pathogen causing superficial to deeply invasive infections in neonates and adults with compromised immunity. Drug resistance is increasing alarmingly in Candida glabrata (a model non-albicans Candida), which need identification of potential molecular targets for the development of new drugs.

Hypoxia is found inside the host tissues, which affects the virulence of pathogen and efficacy of drugs. With an aim to find out effective drug targets under hypoxic condition, thirteen deletion mutants of C. glabrata were characterized in vitro, under hypoxic condition (1% O2). Null mutants were chosen from different cellular pathways, essential for viability and pathogenesis (cell wall biosynthesis, ergosterol synthesis calcium-calcineurin etc.). In vitro growth, biofilm formation and susceptibility of biofilm to antifungal of the mutants were compared with those of wild type control, under hypoxia (1% O2) and normoxia. Hypoxia has reduced the susceptibility of planktonic cells to fluconazole for most of the mutants. Whereas, only few mutants (ecm33Δ, kre1Δ, rox1Δ, and kre2Δ) showed good reductions in their biofilm activities (>20%), when compared to that of control strain under hypoxic condition. In the presence of 16 mg ml-1 fluconazole, selected mutants (upc2B", kre2 ", ecm7", rox1 ", mid1", ecm33", cch1", kre1") have been reported for highly reduced biofilm activities (> 30%), when compared to that of control strain under hypoxic condition. Functional analyses revealed that Kre1, Ecm33, Upc2B, Kre2, Ecm7, Cch1, Mid1 and Rox1 are cellular proteins which can be potential drug targets under metabolic stress, hypoxia.

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Protein identification by matrix-assisted laser desorption ionization (MALDI) Mass Spectrometry

Ankita Gupta[1], Manoj Kumawat[2#], Sushma[2]

1 Divisions of Biotechnology APS vishwavidyalaya Rewa M.P. India.

2 Department of Biochemistry & Biochemical Engineering, JSBB, SHIATS, Allahabad, India.

Division of Veterinary Biotechnology IVRI, UP. India.

Present Address, Correspondence E-mail: manojkbiochem@gmail.com

ABSTRACT

Mass spectrometry (*MS*) is an analytical technique that frequently used in the field of proteomics. Application of MS for the study of proteins is by far the most as compared to the use of MS for the investigation of biomolecules. The term "tandem mass spectrometry" indicates two stages of mass analysis, comprising two key processes: precursor ion isolation and fragmentation of chosen precursor ion. PpiC is a recombinant protein, which contains 93 amino acids. The PpiC protein was subjected to proteolysis by trypsin. The tryptic digest was then characterized by MALDI-TOF MS/MS. The MALDI-TOF MS spectrum PpiC, peaks at m/z 678.40, 765.99, 828.90, 1121.58, 1156.66 and 1396.81 were identified to be due to tryptic peptides from PpiC recombinant protein. MALDI-TOF MS/MS spectra of $[M+H]^+$ of PpiC protein peptide precursor ion m/z 765.99 and 1121.58 subjected to MS/MS analysis. Protein sample sequence was analysis Mascot server. It was found that the PPIase C protein is with a highly convincing score and the sequence coverage is more significant by Mascot analysis.

Keyword: *Mass spectrometry, MALDI, Protein Identification, MS-MS*

Inhibitory mechanism of CPI against viral non structural protein 2: An *in silico* study

Neha Shekhawat , Manali Datta

Amity Institute of Biotechnology, Amity University Rajasthan, Jaipur

E-mail: mdatta@jpr.amity.edu

ABSTRACT

A member of Orthomyxoviridae, influenza virus is the causative agent of respiratory tract illness and is prevalently seasonal. Four types of influenza viruses: A, B, C and D have been discovered with type A being further categorized based on two surface structural proteins of the virus. Non structural proteins (NSP) form an integral part of the viral proteomics and constitute the main machinery for virus replication and maturation. There are five classes of NSP namely NSP1-5. NSP2 has been associated with protease like activity in addition to NTase, RTase and helix destabilizing activities in different viruses. As NSP2 plays vital role in viral maturation restricting the activity would prevent the maturation of virus and thus spread of infection. With this paper, we have explored the interaction of small 13 Kd inhibitor with NSP2 protease domain in silico and studied the binding kinetics of the interaction thus presented.

Keywords: Virus, NSP, Protease, maturation

A liquid chromatography–tandem mass spectrometry approaches for peptides and proteins

Manoj Kumawat[1#], Sushma Allahwat[1], Varatharajan Sabareesh

1. Department of Biochemistry and Biochemical Technology, SHIATS Allahabad (U. P.) India. 2. Centre for Bio Separation Technology, VIT University, Vellore, Tamil Nadu, India

Division of Veterinary Biotechnology IVRI, UP. India.

Present Address, Correspondence E-mail: manojkbiochem@gmail.com

ABSTRACT

Mass Spectrometry (MS) technology is advancing at a rapid pace, mass resolution, and sensitivity, as well as improved ion separation, detection and dissociation technologies. The powerful mass-spectrometry-based technologies now offer unprecedented insights into the composition, structure, function and control of the proteome, shedding light on complex biological processes and phenotypes. We used Thermo LTQ Orbitrap XL mass spectrometer in our present study. We described current MS approaches in protein characterization, including a bottom-up method for protein identification and quantitative proteomics. Bottom-up method is a widely followed proteomic approach, wherein proteins are investigated through proteolytic peptides. Lysozyme protein was subjected to proteolysis by trypsin, and then the resulting tryptic peptides are subjected to liquid chromatography coupled to mass spectrometric characterization (LC-MS). We detected tryptic two peptides SSGTSYP-DVLK (m/z 1153.58) and SGIQVR (m/z 659.39) results from auto-proteolysis of trypsin. The sequences of these two peptides were confirmed by LC-ESI-MS/MS spectra. This data suggests a good example of enzymatic mis-cleavage.

Key words: Mass Spectrometry, LTQ Orbitrap XL, LC-MS, Tandem mass spectrometry

To find out better morphotype among 16 morphotypes of *Jatropha curcas* by *in vitro* regeneration using shoot apices

Sweta Upadhyay, Pramila Shah, Ranjit Singh

Defence Institute of Bio- Energy Research (DIBER), DRDO, Haldwani, Uttrakhand, INDIA.

ABSTRACT

Introduction: The plants of *J. curcas* are drought-resistant shrubs or trees, and are recognized as potential biofuel crop (Jones and Miller 1991; Openshaw 2000). All parts of the plant, including seeds, leaves and bark, fresh or as a decoction, are used in traditional and folk medicine and veterinary purposes (Duke 1988).

Material required: 16 morphotypes of *J. curcas* were collected from DIBER, DRDO Haldwani. MS media was used for *in vitro* regeneration. Different hormone combinations of auxin and cytokinin were used.

Method: Embryos were separated from seeds; they were germinated followed by the shoot apices induction step. Shoot apices were kept in (MS+BAP) for shoot multiplication and shoot elongation. Further transfer to rooting media for rooting.

Result: Embryos were germinated after 4-5 days of dark incubation; they were transferred to light provided by cool and florescent lamps in culture room. After 10- 12 days of light incubation, shoot apices were transferred to media containing 0.5ppm BAP, multiple shooting were observed and then multiple shoots were cut and separated and transferred to individual tubes for shoot elongation. The length of elongated shoots were observed and recorded after 2 weeks elongated shoots were further transferred to the rooting media (MS+IBA). Root initiated within 10-15 days.

Conclusion: The species is primarily propagated through seeds but economic yield comes only after 2-3 years of plantation. Seed viability and rate of germination are also low & quality seed production is a laborious task, thus seed propagation alone cannot provide quality planting material for sustainable use. Mass propagation is only possible through *in vitro* regeneration, a powerful tool for tissue culture. On the basis of germination percentage, shoot length, and root initiation of 16 morphotypes, J16 was found better among 16 morphotypes.

In silico method for DNA-Protein (Histone-based Chromatin) complex Exploration in Archaea

Alok Kumar Singh[1*], Anil Kumar Singh[2], Alok Kumar Shrivastava[3]

[1,3]ICAR-National Bureau of Agriculturally Important Microorganisms, Kushmaur, Mau nath Bhanjan, U.P., India – 275101

[2]Environmental Microbiology Lab, Environmental Toxicology Group

CSIR-Indian Institute of Toxicology Research (CSIR-IITR), Vishvigyan Bhawan, 31, Mahatma Gandhi Marg, Lucknow-226001, Uttar Pradesh, India

[2]Academy of Scientific and Innovative Research (AcSIR), CSIR-IITR, Campus Lucknow- 226001, Uttar Pradesh, India

Corresponding author: Alok Kumar Singh*alok_singh8409@yahoo.com

ABSTRACT

Archean derived proteins have significant biological functions in archaeal cell. Some proteins are most useful in terms of biotechnology aspects. Some small basic proteins present in Archean genetic materials. Histone based chromatin complex formed with participation of this small protein. Histone-DNA complex formed with protein-DNA interaction, this complex is super helix with comprising same geometry as DNA found in the eukaryotic nucleosome. This complex being visualized for DNA-protein interaction with secondary and tertiary protein structure visualization. Structures are predicted for different interaction pose of this complex which explored geometry and different structural views. We found three A, B, C chains in complex while DNA wrapped around the chains. Ligand also found with interacting protein chains which being visualized in predicted structure.

Keywords: *Archaea, DNA-Protein complex, Tertiary structure, PyMOL, DNA-Protein Interaction*

In silico structural analysis for ligand binding site exploration of bacterial derived chrR Enzyme

Ashutosh Yadav[1*], Anil Kumar Singh[2, 3], Pankaj Chowdhary[1], Abhay Raj[2], Ram naresh Bharagava[*1]

[1]Department of environmental Microbiology, Babasaheb Bhimrao Ambedkar University (A Central University), Vidhya Vihar, Rai Bareilly Road, Lucknow uttar Pradesh 226025, India

[2]Environmental Microbiology Laboratory, Environmental Toxicology Group, CSIR-Indian Institute of Toxicology Research (CSIR-IITR), vishvigyan Bhawan, 31, mahatma Gandhi Marg, lucknow-226001, Uttar Pradesh, India

[3]Academy of Scientific and Innovative Research (AcSIR), CSIR-IITR, Campus Lucknow- 226001, Uttar Pradesh, India

Presenting author: Ashutosh Yadav*, Email ID - ashutoshyadav.shalu@gmail.com

ABSTRACT

Hexavalent form of chromium [Cr (VI)] is toxic heavy metal to human and animal health. Bacteria are the key source of reduction of hexavalent form of chromium into its simplest form. Currently bacteria are being focused for chrR enzymes involving in catalysis and transfer of three electrons to Cr^{6+} producing Cr^{3+}. three-dimensional structure of chromate reductase protein provides its constituents specific amino acid arrangement in its structure. Structure prediction and analysis of protein model for different chemical properties was performed Through online server (http://swissmodel.expasy.org/workspace/)SWISS-MODEL Workspace, is an automated online server for comparative modelling. Modelling of chromate reductase enzymes being performed after retrieving sequence of amino acids. Two methods are available one is manually and other one is automated mode for protein modelling. Automated mode is best suited and perform itself for best scoring model with different default parameters. Completion of modeling process modeled pdb file has the coordinates information of all atoms present in chrR molecule. Modeled file subjected to visualization of three-dimensional structure and its ligand binding site exploration. PyMOL is a best suited molecular graphics visualization software utilized for high quality model structure prediction in different form. Active site for ligand binding to chromate reductase explored by using of PyMOL which revealed constituent's amino acids present in active site around the ligand and their interaction with active side residues.

Keywords: ***3D structure, Binding site, Active site prediction, Molecular visualization, Ligand.***

***Corresponding Author: Dr. R. N. Bharagava**

Tel: (+91) 522-2998718; Fax: (+91) 522-2441888

E-mail: bharagavarnbbau11@gmail.com, ramnaresh_dem@bbau.ac.in

Structure-function characterization of β2-microglobulin in study of hemodialysis related amyloidosis

Devanshu Mehta and Tapan K. Chaudhuri
Kusuma School of Biological Sciences, Indian Institute of Technology, Delhi, New Delhi, India email: devanshumehta01@gmail.com

ABSTRACT

Many proteins require proper structure to be functional inside cells. Cellular machinery strives to prevent protein misfolding and also mediates proper disposal of misfolded proteins through the proteasomal degradation pathway, thereby facilitating cellular survival. However, in certain cases, misfolded and mutated proteins accumulate resulting in the formation of a certain type of aggregate called amyloid fibrils. These fibrils adversely affect the structure and function of tissues and organs that come in contact with them, causing amyloidosis.

In our effort to understand such events of protein misfolding and amyloidosis, we have chosen to study Dialysis-related amyloidosis (DRA). DRA results in patients suffering from renal failure and later subjected to prolonged haemodialysis. It involves the accumulation of misfolded β2-microglobulin (β2m) specifically in the musculoskeletal system of the human body. β2m, a light chain protein component of MHC class-I molecules, is expressed on the surface of all nucleated cells. It is normally shed off into the serum as a part of a normal turnover exercise and is metabolised by the kidney in a healthy individual. However, in patients with renal failure, the serum concentration of β2m increases sixty fold leading to its associative accumulation into bones and surrounding areas. The asymptomatic first β2m amyloid deposits appear in the cervical intervertebral discs after three years of dialysis. DRA becomes symptomatic only after five years of dialysis with painful joints, Osteoarticular (bones & joints) complications, chronic arthropathy, cystic bone lesions, destructive arthropathy, pathologic fractures, scapulohumeral periarthritis and others. Our study involves characterising effects of potential inhibitors to combat β2m mediated amyloidosis and to reduce serum population of misfolded β2m in ESRD patients subjected to hemodialysis.

Effect of leaf-applied some essential nutreints on juice purity percentage in ten sugarcane (*Saccharum officinarum L.*) cultivars

***Singh J.and Abbas Z**
P.G.Department of Botany, G.F.College, (M.J.P.Rohilkhand University), Shahjahanpur,242001, U.P.,INDIA
e.mail:-jagjitsinghsidhu63@gmail.com, *Research scholar

ABSTRACT

In a field trial conducted during 2014-2015(spring planting) at G.F. College, Shahjhanpur,(U.P.),India to study the effect of 1% foliarly applied aqueous solutions of Zinc sulphate, Magnesium sulphate, Potassium nitrate, Potassium sulphate and Potassium meta-silicate and 0.2% aqueous Boric acid spray solution applied at post mansoon (180 DAP) stage as compared to foliarly applied water only (control) in ten sugarcane varieties (CoS 95255, CoS 96268, CoSe 98231, CoS8436, CoSe01235, CoS94257,CoS767,CoS97261, CoS97264 and CoS99259) was studied.. The juice purity percentage was noted at harvest only.The purity of the juice showed positive response to all the treatments significantly. Potassium sulphate,Potassium nitrate and sodium-metasilicate segnificantly showed low value of juice purity.Regarding varieties CoS 94257,CoS 97267,and CoS 97261,recorded lower values for juice purity percentage.Most of the treatment combination with CoS 96268 and CoS 95255 varieties gave higher values of interaction s as compared to others for this juice quality parameter.

Key words :- juice quality, essential nutrients, sugarcane.

Biodegradable Microparticles Containing Potent Chemotherapeutic Agent for Targeting Cancer Cells

Kriti Dixit, Mustufa Khan, Raj Vardhan Tripathi, Tarun Upadhyay*
[1]Department of Life Science, Institute of Applied Medicine and Research, Delhi-Meerut road, Ghaziabd (U.P)-201206
*Email: kritidixit95@gmail.com, tarun.upadhyay@iamr.ac.in

ABSTRACT

Introduction: Cancer is the second most common disease worldwide. It was envisaged to develop microparticles (MPs) containing an Anticancerous drug such as methotrexate (MTX) to target cancer cells.

Materials and Methods: MPs prepared from biodegradable polysaccharide source. These formulation were compared with MTX loaded MPs (MTX-MPs). The Prepared formulations were investigated for size distribution, zeta potential, *In vitro* drug release profile and uptake studies.

The trypan blue dye exclusion assay and *insilico* ADMET analysis were performed to check the cytotoxic potential of the prepared formulation.

Results: The microparticles have been found to have an average size in the range of 1-5 µm in diameter and having polydispersity index (PDI) of 0.169 indicating mono-dispersity of carrier system. The zeta potential of the microparticles was found to be −24.6 mV. The percent growth inhibition of prostate cancer cells (PC-3) with MTX-MPs was found to be better than MTX alone indicating that receptor mediated uptake of the drug. *In-vitro* cell viability assay and cell uptake studies were performed to assess the preferential role of MPs in cancer targeting.

Conclusion: These studies provide evidences that such drug delivery systems holds promise to address cancer cells over-expressing receptors. This carrier based formulation play dual role of having propensity to release the drug in the tumour environment, better localization and targeting with improved therapy due to over-expression of receptors.

Keywords: Methotrexate (MTX), Microparticles (MPs), Prostate cancer

Identification of Microsatellite markers and FDM analysis through EST sequences of *Astraeceae* family

Monali Mishra, Sangita Dixit and Souvagyalaxmi Sahoo*

Tectona Biotech Resource Centre, Bhubaneswar, Odisha-751002

Email: souvagya.tbrc@gmail.com contact no-9337524676.

ABSTRACT

The plant of *Astraeceae* family are an important medicinal plant, but application of molecular markers in this family yet to gain momentum. A simple sequence repeat–functional domain marker (SSR-FDM) relies on the development of molecular markers for putative functional domains using simple sequence repeats and in-silico annotated information of those sequences using biological databases. In this study, the expressed sequence tags (ESTs) of the *Astraeceae* family were analyzed for in-silico mining of EST-SSRs, SSR-FDM analysis, functional annotation, and open reading frames (ORFs). The EST sequences of *Astraeceae* family were retrieved in FASTA format from dbEST database of NCBI for SSRs development. These FASTA format sequence were subjected to preprocessing using trimest and vecscreen tool. The trimmed EST sequences were subjected to assembly using CAP3 (http://biosrv.cab.unina.it/webcap3/) assembler. The unique EST sequences i.e. contigs and singletons which were obtained from CAP3 were further harvested for microsatellite sequences using MISA (MIcroSAtellite identification tool). A pair of primer flanking each SSR was designed using Primer3 software which is freely available with MISA. Open reading frames (ORFs) are predicted for all the SSR containing sequences using ORF finder available at NCBI using standard genetic code. SSR-FDM analysis were done by using Interproscan and blast2GO tool for Gene Ontology terms and annotation. A total of 1598 EST sequence of the Astraeceae family were downloaded from database of dbEST (NCBI). Further these sequences were analyzed for tandem repeats. After analyzing the sequences were subjected to trimming of poly A/T tails and removal of vectors. We identified around 580 sequences were assembled, which resulted in 142 contigs and 1018 singletons. Analysis of EST-SSRs revealed mononucleotide SSRs to be the most common, at 87.34 %, with dinucleotide SSRs accounting for 4.77% and trinucleotide accounting for 7.88% of all data. Assembled sequences yielded 482 SSR's in contigs and singletons. Out of a total of 482 identified SSR-ESTs only 235 SSR-ESTs were successfully annotated using Gene Ontology terms. These 482 SSR-ESTs were subjected to primer designing which yielded a total of 69 primer sets for astraeceae family. The sequences having both SSRs and FDMs signify that functional domains provide predicted functions to the molecular markers. The EST-SSRs developed in the present study will be help to analyze molecular markers that have functional importance. This study provides a brief idea about the approach to develop computationally mined SSRs from ESTs and should also facilitate the analysis of genetic diversity in plants especially medicinal plants.

Key words: *Astraeceae*, simple sequence repeats (SSRs), Expressed sequence tags (ESTs), functional domain marker (FDM), In silico analysis.

Isolation and purification of a protease inhibitor from guar seeds

Preeti Patidar[1], Rajesh Rawaliya[1], Sumati Hajela[2] and Krishnan Hajela[1]

[1.] School of Life Sciences, DAVV, Indore .MP.452001

[2.]Dept of Biotechnology, IPS Academy, Indore MP 452001

preeti.patidar1988@gmail.com

ABSTRACT

Substances having the ability to inhibit the proteolytic activity of certain digestive enzymes are found throughout the plant kingdom and particularly in legumes. There is continued interest in the possible use of plant proteinase inhibitors in treatment of wide range of metabolic disorders which are associated with enhanced proteolytic activity.(e.g. pancreatitis, allergy, inflammation and certain cancers). Here

we discribe about the isolation and purification of inhibitor from guar seeds(Cyamopsis tetragonoloba). Guar is a major source of a gum, a galactomannan which have several industrial applications .There have been no studies on isolation and purification of protease inhibitor from guar seeds. So we attempted to isolate and purify aprotease inhibitor. For the isolation and purification of protease inhibitor from guar seeds Seeds were soak overnight in phosphate buffer pH 7.5 ,then homoginised in same buffer and upernatent collected by centrifugation at 10000 rpm for 30 minutes .This supernatent was heated at 60° C for 20 minutes and after cooling precipitated by 80% ammonium sulphate and desalted by a G-25 column .The protein was further purified by DEAE -cellulose column and inhibitory activity was checked in isolated fractions using tyrypsin as enazyme and BAPNA or casien as substrate. The molecular weight of protein was determined by SDS PAGE. Glycosylation of protein was checked by Dubois method and PAS staining. The yield of protein was found to be 0.02% only . The molecular weight of protein under non reducing conditions was found to be 11KDa .On reduction lower bands were obtained. The protein was found to be glycosylated with 23 ug sugar per mg of protein. Sialic acid was not present.About 10ug of purified inhibitor inhibited 0.4 ug of Trypsin completely. Guar seeds contain a low molecular weight heat stable Bowman Birk trypsin inhibitor.

Structural properties of unboun Argonaute protein in contrast to the guide RNA bound complex

Richa Anand*

Corresponding author: Richa Anand, Indian Institute of Information Technology Allahabad , Email: richaaanand@gmail.com)

ABSTRACT

RNA interference (RNAi) is a biologically conserved phenomenon which regulates the expression of genes through transcriptional and post-transcriptional gene silencing mechanism. It is triggered by small double-stranded RNA molecules. The pathway involves a network of proteins to recognize nucleic acid and then cleavage of target mRNA. The key player of this pathway is Argonaute proteins (Ago). In recent years, a number of structural studies provided insights into the molecular architecture of Ago proteins. In this work, two molecular dynamics simulations followed by hydration study of guide RNA bound Ago protein and unbound Ago protein in the presence of molecular crowders was carried out. The protein, PDB ID: 4W5N, was taken for this work. It was observed that hydrogen bonding and water molecules play a crucial role in the structural integrity and dynamics of the Ago protein complex. The study revealed the important role played by interfacial water networks towards the physiological function.

Keywords: RNAi, Molecular dynamics simulation, Argonaute protein family.

An attempt to understand the population genetic structure of related cattle species of Asian subcontinent using a genomic approach

Sheikh Firdous Ahmad[1*], Manjit Panigrahi[2] and Bharat Bhushan[3]

1-PhD, 2- Scientist (SS), 3-Principal Scientist

Division of Animal Genetics, ICAR-Indian Veterinary Research Institute, Izatnagar, Bareilly 243122, UP, India,

***Correspondence –** firdousa61@gmail.com

ABSTRACT

Genetic characterization of livestock species/subspecies/populations has become an important part of population genetics' studies. It has become a reality mainly due to the availability of high-throughput technology, BeadChips and easy genotyping on a genome-wide basis. In this study, we have used 50K SNP genotypic data for a total of 111 animals belonging to four different, but an evolutionarily related subspecies of cattle to study the population genetic structure and infer a possible evolutionary relationship. Besides, three out-group breeds of Banteng (2), Indian Bison (4) and Yak (2), seven popular cattle breeds of the Indian subcontinent were also used in this study, namely, Sahiwal (17), Hariana (10), Kankrej (10), Gir (24), Ongole (20), Tharparkar (12) and Red Sindhi (10). We have taken 29,737 filtered SNP variant markers, common to all populations under study for the analysis. The average minor allele frequency was observed to be 0.163 ± 0.002. Polymorphic and fixed SNPs were found to be distributed uniformly across the genome as depicted by chromosome-wise marker coverage. The genetic structure of three

out-group populations was found to be distinct from breeds of Zebu inheritance. The breeds of Zebu lineage were separated into different levels based on genetic structure studies under Bioinformatics' approach. The approach of principal component analysis (PCA) also separated the out-group species from breeds of Zebu cattle. The first two principal components explained 7.97 and 4.96 % of the total variation, respectively.

Keywords: Genetic structure, Out-group, PCA, PLINK, SNP, STRUCTURE, Zebu

In- Silico Comparative structural analysis of 5-HT2A receptor in Homosapiens

Soni Singh, Alok Jha

Department of Biotechnology and Life Sciences, Mangalayatan University,Extended NCR 33rd Milestone, Aligarh-Mathura Highway, Beswan, Aligarh-202145, India.

ABSTRACT

Serotonin is a neurotransmitters present at the synapses of nerve cells. 5-HT2A receptor is primarily involved in transport of serotonin molecule from nerve cell to extracellular fluid as well as its reuptake. In the Central nervous system, serotonin molecule is involved in regulation of sleep, depression, anxiety, aggression, appetite, temperature and pain sensation. In the present study we have performed a comparative study of four different models for 5-HT2A receptor modeled by different softwares. The study involved 5-HT2A homology Model prediction by: Modeller 9.14, Swiss Model server, Phyre2 and Geno3D. The homology models of 5-HT2A were evaluated by ERRAT from Procheck, Qmean score from SwissModel server, and Ramachandran Plot analysis by RAMPAGE. Validation and verification showed that the models build by SwissModel is of acceptable quality.

Keywords: Serotonin, 5-HT2A, Homology Modelling, Ramachandran Plot

Extracellular Calcium Concentration Mediates Disorder To Order Transition And Functional Processing Of Serralysin

Vishal Srivastava, Tapan K. Chaudhuri

Kusuma School of Biological Sciences, Indian Institute of Technology Delhi, Hauz Khas, New Delhi-110016, vsri.iitd@gmail.com

ABSTRACT

Apart from a few genera of enterobacteriaceae such as *Pseudomonas, Serratia, etc.*; no true secretory system exists in Gram negative microorganisms. Secretome of these specific genera comprises of protein molecules which act as virulence factors. These virulence factor either show cytotoxic activity or act as hydrolases degrading lipids, carbohydrates, nucleic acids and proteins.

Serratia marcescens; a known opportunistic pathogen, common in nosocomial infections secretes at least five different type of proteins including two different proteases. The major metalloprotease in *Serratia marcescens* secretion, also known as serratiopeptidase acts inherently as a virulence factor but is also widely used in therapeutic combinations for its anti-inflammatory, analgesic and anti-edemic effects. The protein shows structural features characteristic of Repeat-in toxin (RTX) protein family having a two-domain architecture. The N-terminal proteolytic domain (PD) having canonical HE*XX*H*XX*G*XX*H zinc binding motif forms the catalytic site of protein. The C-terminal calcium-binding domain consists of nonapeptide glycine and aspartate-rich repeats. Repeat-in toxin sequences are known for forming ordered β-rolls in presence of adequate calcium ion concentration.

Our work enforces the proposed hypothesis that in the absence of calcium, the intrinsically disordered structure of RTX proteins assists in the secretion of protein moieties. It suggests that its function may be conserved and is independent of the specific enzymatic activities associated with the particular exoprotein. Calcium ions in the micromolar concentration range (abundant in extracellular environment) assists the binding of divalent calcium ions to multiple sites in C-terminal RTX domain causing a disorder to order transition of protein molecules. This type of calcium and protein interaction not only helps in folding of the particular C-terminal domain which extends into the vectorial folding of complete holoenzyme but also the pro-peptide processing and activation of zymogenic version.

Keywords: Repeat-in Toxins, Serratia marcescens, Serratiopeptidase, Vectorial folding

Genomic Diversity Of Ladakhi Tribal Population A Cultural Haritage With Buddhist Tibetian Poppulation

Shashank Upadhyay [1*], Shivendra Upadhyay [2], R.C.Gupta [3], V.K. Singh [3], Gaurav Gupta [4]

1. Department of Biotechnology, Invertis University, Bareilly- Lucknow National Highway-24, Bareilly-243123, India
2. A.K.G Engineering College, A.P.J, U.P. Technical University, Luck now.
3. V.B.S Purvanchal University Jaunpur ,U.P.
4. .Genome Foundation, Osmania University Main Rd, Amber pet, Hyderabad, Telangana 500007

Email: Shashank.u@invertis.org

ABSTRACT

Ladakh India is a well-diversified genetic hub with a conserved population structure, a pluralistic society is a diverse one not only in food practice but also in marriage system, where the people in it believe all kinds of different things and tolerate each other's beliefs even when they don't match their own. "Human populations alter one from another around entirely in the deviating *proportions* of the allelic genes of the discrete sets of hereditary factors, and not in the variety of genes they enclose" (Zeng *et al.,* 2006). Human populations can be characterized on geographic, political, linguistic, religious, or ethnic horizons (Sawyer and Hartl, *et al* 1992).India, the world's second most populous nation is uniquely recognizable for its mixed diversification. Be it geographic or climatic dissimilarity, be it the dissimilarity in languages, religions, and cultures of its people, or be it the genetic dissimilarity as conspicuous today, after all, it is our authentic diversity that conveys strength to our individuality (Reich *et al.,* 2009, Priya *et al.,* 2013). The phylogeny of the indigenous Indian-specific mitochondrial DNA (mtDNA) haplo groups have been determined in various reports. On account of versatile wide range of disciplines viz demography, history, linguistic and genetic architecture, Ladakh tribal population offers a platform to study the clustering in population diversity from the rest of India. The original LADAKH people were supposed to be the DARDS, an Indo-Aryan race down from the Indus and the GILGIT area. Immigration from the Tibet replaced the genetic architecture of the Dards and conserved due to the climatic barrier of Ladakh region, bounded by two world highest mountain ranges namely karakoram and Ladakh range of India. Our mitochondrial DNA analysis shows some significant evidence for the origin of pre-historic hierarchal tribal society of ladakh region. The racial inbreeding between the local populations had conserved the genetic diversity in a limited area, due to no outsourcing of gene pool. The expansion of tribal population and gene flow is constant hence, numbers of tribes are static. (K. Thangaraj , *et al* 2009 PLoS ONE) The history of Ladakh prior to the birth of the kingdom in the 1Oth century is limited. The present-day population of Ladakh is composed of mixed races. The main among them are the Indo-Iranic race, the Tibetan race and the Mongoloid race According to the Ladakhi Chronicles and some other sources, the earliest inhabitants of Ladakh were composed of the Mons and the Dards.1 They migrated to Ladakh at an early time, but it is difficult to fix an exact date. According to Petech the earliest population of Ladakh was composed of the Dardis.2 According to A. H. Francke the Mons came from India. 3 As far as the Dards are concerned, they migrated to Ladakh from Gilgit.4 The remains of contemporary Dardis are still found in Dha-Hanu,Darchik and Garkon in Lower Ladakh. The Dards are believed to belong to the Aryans race. The last ethnic group mainly Mongols of Tibetan origin came in the 8th and 9th century and which is the dominant ethnic group in Ladakh at present It is believed that Buddhism was first introduced to Ladakh from Kashmir during the reign of the emperor Ashoka. The great Ashoka who adopted Buddhism as his state religion, zealously spread it throughout not only his own empire but also sent missionaries to neighboring countries. It is believed that Ashoka also sent missionaries to Ladakh.5 When the third Buddhist council was held by king Ashoka (272~232B.C.), it was resolved to send Buddhist missionaries to Yarkand, Kashmir and many other countries. Buddhism got such a firm foothold in Kashmir that the fourth Buddhist council, under the King Kanishka (125-152 A.D.), is said have to been held in Kashmir. According to Francke, either after the third or the fourth council Buddhism have been carried to western Tibet, situated between Kashmir and Y arkand. 6 The remains of the Kashmiri influence can still be seen in Ladakh. The Stupa at Sani and the ancient sculpture at Padum in Zanskar are believed to be from that period. The statue of Maitreya Buddha at Mulbhe, which is about 40km' before Kargil, is another monument of Kashmiri influence In In fact it is quite possible that the inhabitants of Ladakh felt the Tibetan influence even earlier, for the nomadic Tibetans of Changthang would· have good reason to have contacts with the Mon and Dard, exchanging grain for animal products. The Tibetan nomads occupied the higher pasture ground for their animals and the Aryan tribes (Mons· and~ Dards) irrigated in the lower plains. By the mid-seventh century, during the reign of the King Songstan Gampo in Central Tibet, Ladakh became increasingly aware of her eastern neighbour. During this period the Tibetan nomads of Changthang probably inter-married with the Mon and Dard population and allowed a trading or bartering system to develop between the two groups of people. Before the origin of the first Ladakhi dynasty in the 1Oth century by Skid ide Ni-ma-mgon, it is said that Upper Ladakh was under the descendents of Gesar and Lower Ladakh was divided into small principalities. According to the Chronicles of Ladakh, Skid-ide Ni-ma-mgon had three sons, dPal-gyi-ide-mgon, b:Kra-sis-mgon and third one. The origin, evolution and migration have surveyed the Ladakhi history from early years to the end of the first dynasty rule in Ladakh. It is certain that before the Tibetan influence, the cultural influence on Ladakh was from Kashmir but far too little remains except some rock carvings. The first important and widespread cultural impact from Tibet came with the establishment of the first Ladakhi dynasty rule in the tenth century. During this period emphasis was on the patronage and support of construction of monasteries and stupas in Ladakh. Besides, the Kingdom's patronage of Tibetan Buddhism, L!lffia missionaries also played an important role in the spread ·of Mahayana Buddhism. Ladakh's religious and spiritual matching with Buddhist Tibet during this period were close and consistent.

Keywords: Admixture, Phylogeny, Indigenous, mt-DNA, Indo-Aryans Diversified, Conserved, Novel, changthang, religious.

The MSMEG_3955 flavoprotein from *Mycobacterium smegmatis* contains FMN as a cofactor

Neha Khosla, Sharad Thakur, Seema Madhumal Thayil and Anup Kumar Kesavan*
Department of Molecular Biology and Biochemistry, Guru Nanak Dev University, Amritsar

ABSTRACT

In *Mycobacterium tuberculosis* the dormancy survival regulator (DosR) regulon is composed of 48 co-regulated genes. One of gene Rv3131, a hypothetical protein is upregulated during stress and hypoxic condition is Rv3131. The functional homologue of this gene in *M. smegmatis* is MSMEG_3955. The role of MSMEG_3955 is still unknown. In this regard characterization of this flavoprotein was undertaken. PCR, Cloning, Expression and Purification of protein (MSMEG_3955) : PCR was used to amplify MSMEG_3955 gene from whole genome of *M. smegmatis MC2 155,* with the help of gene specific primers. The PCR product was cloned in the expression vector (pET-28a) and transformed into *E. coli* (DH5α). For protein purification, the plasmid was transformed and expressed in *E. coli* (BL21) (DE3). Ni-NTA affinity chromatography was used to purify protein. SDS-PAGE and NATIVE PAGE analysis: The molecular weight of protein MSMEG_3955 was confirmed by SDS-PAGE under denaturing condition and native PAGE was used for under non denaturing conditions. Circular dichroism: The secondary structure of protein MSMEG_3955 was evaluated by using Circular Dichroism Spectroscopy. Fluorescence Spectroscopy: The presence or absence of flavin cofactor was determined by Fluorescence Spectrosccopy. UV spectroscopy and Thin Layer Chromatography: The type of cofactor (FMN/FAD) bound to holoprotein was determined by UV spectroscopy and TLC. By using gene specific primers a PCR product of size ~1005 bp was obtained. The PCR product was cloned into the expression vector pET28a using appropriate restriction enzymes. SDS-PAGE analysis of the purified MSMEG_3955 protein was ~36KDa. Native-PAGE analysis showed that the MSMEG_3955 protein is homotrimer, with a protein size of ~115KDa. Circular Dichroism spectroscopy of protein MSMEG_3955 showed α-helix 18.4%, β-pleated sheets 24.9%, Turn is 19.1% and random coils at 37.7%. Fluorescence Spectroscopy showed the presence of flavin as the cofactor. UV-Spectroscopy and Thin Layer Chromatography confirmed that the cofactor bound to the protein MSMEG_3955 was FMN.

Study on Validation of different IPM Modules against Okra Shoot and Fruit Borer

Jitendra Kumar Rawat*, Anoorag Rajnikant Tayde**
Department of Entomology SHUATS Allahabad, India.
**Email : rawat.jitendra08@gmail.com*

ABSTRACT

Okra (Abelmoschus esculentus L.) is an economically important vegetable crop grown in tropical and sub-tropical parts of the world. This crop is suitable for cultivation as a garden crop as well as on large commercial form. One of the major constraints identified in okra production is the increasing incidence of insect pests, disease and nematodes, resulting in substantial yield losses. The experiment was conducted Randomized Block Design with three replications and ten treatments. The effect of all the sprays indicated that the module M4 composed of Endosulfan 35 EC (0.06%) followed by B. thuringiensis var. kurstaki @ 1.5 g L1 followed by Maharukh leaves extract 10 ml aqueous solution L-1 recorded lowest fruit infestation of 15.89 %. However, the module M3 (Endosulfan 35 EC 0.06 %) followed by B. thuringiensis var. kurstaki @ 1.5 g L-1 followed by Serni leaf extract 10 ml aqueous solution L-1), module M9 (Cypermethrin 10 EC 0.005 %) followed by NSKE 5 per cent followed by custard apple leaf extract 10 ml aqueous solution L-1), module M5 (Deltamethrin 0.09 %), followed by Neemazal 4 ml L-1 followed by Soapnut 10 ml aqueous solution L-1), module M8 (Profenofos 50 EC 0.05 %), followed by NSKE 5 per cent then garlic and chilli extract 10 ml aqueous solution L-1) composed of alternate spray of chemical and bio pesticides had also recorded nearly low fruit infestation (16.11,16.92,16.38 and 17.02 %, respectively) comparable with module M4. The cumulative effect of all the sprays indicated that the module M9 (Cypermethrin 10 EC 0.005 %) followed by NSKE 5 % followed by custard apple leaf extract 10 ml aqueous solution L-1, module M8 (Profenofos 50 EC 0.05 %), followed by NSKE 5 % then garlic and chilli extract @ 10 ml aqueous solution L-1), module M5 (Deltamethrin 0.09 %) followed by Neemazal @4ml L-1 followed by Soapnut 10 ml aqueous solution L-1), M4 composed of (Endosulfan 35 EC 0.06%) followed by B. thuringiensis var. kurstaki @ 1.5 g L-1 followed by custard apple leaf extract 10 ml aqueous solution L-1 and M3 (Endosulfan 35 EC 0.06%) followed by B. thuringiensis var. kurstaki @ 1.5 g L-1 followed by Serni leaf extract 10 ml aqueous solution L-1 composed of alternate spray of chemical pesticides, bio-pesticides and botanicals have recorded low fruit infestation (17.07, 17.15, 17.20, 17.36 and 17.88 % fruit infestation, respectively) and were at par with each other. Above results revealed that integrated approach consisting of alternate use of chemical pesticides, bio pesticides and botanical can be adopted for the management of okra shoot and fruit borer to reduce the chemical pesticide load on the crop and to decrease residue in okra fruits.

Key words: IPM, Okra, Okra Fruit and Shoot Borer.

Hurdle alleviation for CKD detection: A Step towards healthy lifestyle, Preliminary design and testing of protein sensor

Dignya Desai[1], Manali Datta[1] and Ashok Kumar[2]

[1]*Amity Institute of Biotechnology, Amity University Rajasthan-303007, India.*

[2]*CSIR-Institute of Genomics and Integrative Biology, Mall Road, Delhi-110007, India.*

ABSTRACT

Kidney is one of the most important organs of the body and its main function is filtering the waste products from blood. Chronic Kidney Disease (CKD) is one of the 4th most common kidney disease causes kidney infection, stone formation and kidney cancer. CKD is a worldwide public health issue and it is estimated to effect 1 in every 10 adults in India.

CKD is divided into 5 stages based on the severity of the disease which is determined by glomerular filtration rate (GFR). The present method for detection of CKD are GFR, ultrasound, CT scan , kidney biopsy, creatinine assay, Albumin and blood urea nitrogen estimation. Therefore, a simple, rapid, accurate and economical method is required for to diagnosis of CKD in early stage with high specificity.

The biosensor may be one of the more efficient and sensitive technique for detection of CKD using specific biomarker released in patient urine in early stage of kidney problem. Based on this marker, the nanosensor was fabricated using specific nanohybrid composite of multiwalled carbon nanotube electrode system. Papain , a cysteine protease was used as an aptamer and a biomarker, Cystatin C was used as a targeted molecule. Papain was covalently immobilized and analyzed electrochemically for the detection of the biomarker based on cyclic voltametry. With increase in concentration of CysC concentrations, consistent dip in the current was observed. For CysC concentrations 6.6×10^{-5} ng/µl, 3.3×10^{-4} ng/µl, 6.6×10^{-4} ng/µl, 3.3×10^{-3} ng/µl, 6.6×10^{-3} ng/µl, 3.3×10^{-2} ng/µl and 6.6×10^{-3} ng/µl, consistent changes in the CV profile was observed, thus confirming the success of the designed template. The proposed alternate method may offer a cost effective solution to detection of CKD and its progression. The biosensor thus designed had a good detection range corresponding to Stages I and II of CKD. Further testing based on other electrochemical methodologies need to be performed for confirmatory results.

Keywords: Papain, Cystatin C, Chronic Kidney Disease

PPI STREAMLINED FOR DIAGNOSTICS: A tool for kidney analysis

Manali Datta and Dignya Desai

Amity Institute of Biotechnology, Amity University Rajasthan, India, E-mail ID:*mdatta@jpr.amity.edu*

ABSTRACT

Chronic kidney disease (CKD) is a condition in which gradual loss of kidney function over time. CKD may be caused by diabetes, high blood pressure and other disorders. The present method for detection of CKD are all hospital based analysis based on creatinine. albumin and blood urea nitrogen and are either time consuming or expensive. Current scenario requires utilization of a validated marker which does not have disadvantages associated with creatinine and urea. One such proteinaceous marker present in all nucleated cells, present in all human body fluids and especially abundant in milk cerebrospinal fluid and seminal plasma, it is solely filtered by glomerulus making it an apt indicator of CKD. The basic setup of the kit was designed using a syringe containing multiwalled carbon nanotube (MWCNT) conjugated protease. Casein beads were immersed in phosphate-buffered saline in the syringe. The glass/MWCNT/papain solid support was subsequently inserted into the syringe in such a way that the beads came in contact with the immobilized enzyme conjugate. The inhibitory action of cystatin C against protease forms the basis for the functioning of the kit. Results indicated that papain while immobilization needs to be in dynamic conformation. At 37°C, papain gave better activity as compared to protein immobilized at 4°C. Fourier transformation infrared spectroscopy observations confirmed the physical adsorption on the MWCNTs. The experimentation confirmed the feasibility of using prototype for detection of cystatin C. The proposed alternate method may offer a cost effective solution to detection of CKD and its progression. The initial design of the diagnostic kit for the detection of CKD has shown to be successful with a good detection range corresponding to Stages I and II of CKD. Further testing needs to be done for the prototype using patient samples

Keywords: Papain, Cystatin C, Chronic Kidney Disease

In-silico Identification of Inhibitors for 1-cys Peroxiredoxin of *Plasmodium falciparum*

Prashant Kumar[1],Saurabh Gupta[2], Pritish Kumar Varadwaj[2],Ashutosh Mani[1]

Department of Biotechnology, MotilalNehru National Institute of Technology, Allahabad,

Department of Applied Sciences,Indian Institute of Information Technology, Allahabad

Email;kumar.prashantbds@gmail.com

ABSTRACT

Despite of global efforts for eradication of malaria the deaths caused by the disease is a matter of concern. Increasing range of drug resistance reports in *Plasmodium falciparum* has emphasized the necessity to spot new drug targets within the parasite. Malaria remains one of the most challenging human infectious diseases, with a high rate of resistance outbreaks and a constant need for the discovery of novel antimalarial and drug target. Initially by using different sequence analysis steps the target sequence has been identified and modelling of the protein sequence was performed by using MODELLER.Subsequently the natural compounds from different databases such asAfroDb,Analyticon, Npact database,Nubbe natural products, Princeton natural productswere downloaded and natural product database created of size 36968 using Phase Schrödinger.Further virtual screening and docking was performed using GlideSchrödinger.Finally molecular dynamic simulation and analysis of best Protein ligand complex was performed for 50 nanosecond using Desmond.Through array of sequence analysis for suitable target identification in *Plasmodium falciparum* we have identified the recently characterize protein, 1-cys Peroxiredoxin (XP_001349492) was selected as a drug target for lead compound identification. Further virtual screening and docking of natural inhibitors indicates the compound forming best complexes with above said target protein.Moreover dynamic simulation of best complex Zinc49180909 illustrate the inside interaction analysis in presence of real time environment. The identified inhibitor may be used as a lead compound for discovery of antimalarial drug.

Key Words:*Plasmodium falciparum*,Antimalarial,Docking,Dynamic simulation

An overview of Protein/DNA interaction in multifarious DNA topologies

Saurabh Kumar, Himani Patel and Sakshi Dubey

Department of Botany, Khandelwal College of Management Science and Technology, Bareilly, *E-mail: saurabh_k02@rediffmail.com

ABSTRACT

Specific interactions between proteins and DNA are fundamental to many biological processes. In this article, we provide a revised view of protein-DNA interactions that emphasizes the consequence of the three-dimensional structures of both macromolecules. Protein-DNA interactions divided into two categories: those where the protein recognizes the unique chemical signatures of the DNA bases (base readout) and those where the protein recognizes a sequence-dependent DNA shape (shape readout). Further Protein/DNA interaction divide base readout into those interactions that occur in the major groove from those that occur in the minor groove. Analogously, the readout of DNA shape is subdivided into global shape recognition, for example when the DNA helix exhibits an overall bend, and local shape recognition, for example when a base pair step is kinked or when a region of the minor groove is narrow.

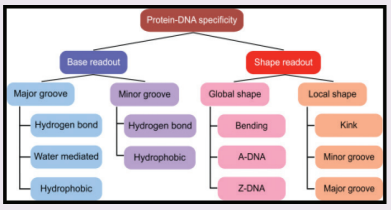

Figure: Base recognition in the major and minor groove

Base readout: One ingrained way for proteins to attain DNA binding specificity is through interactions with the bases in either the major or minor groove that distinguish the chemical Signature of the base or base pair. This type of recognition is generally mediated by the formation of hydrogen bonds between amino acids and bases, which convey the highest degree of specificity, and, in some cases, by water-mediated hydrogen bonds, or hydrophobic contacts.

Shape readout: For most DNA binding proteins, the readout of base pairs is not sufficient to explain specificity. Other factors that have been proposed to contribute to specificity are sequence-dependent DNA structure and deformabilit. These readouts, which all depend on deviations from ideal B-DNA, comprise a diverse set of mechanisms that all fall under the general heading of binding a non-ideal B-DNA shape. As such, we collectively refer to them as *shape readout*. Further, we distinguish between *local shape readout* mechanisms, in which the DNA

helix deviates from ideal B-DNA in a localized manner, and *global shape readout* mechanisms, in which most of the DNA binding site is either deformed or in a non-ideal B-form conformation. Both local and global shape readouts can contribute to DNA binding specificity. For local shape readout, such as minor groove narrowing, recent results suggest that the shape of the minor groove within a binding site can be "read" by a complementary set of basic side chains. In contrast, global shape readout, such as a gradual bend in the DNA helix, may position elements of the DNA backbone such that these otherwise non-specific contacts can become highly specific.

Global shape readout: We include in this category the recognition of DNA sequences where the entire binding site is not in a classic B-form helix. Examples are the recognition of bent DNA, where the curvature is distributed along the entire helix, A-DNA, sequences that have elements of both A- and B-DNA, and Z-DNA.

Local shape readout: As described in the DNA structure section, the two predominant local shape deviations from ideal B-DNA. are 1) small regions of 3–8 base pairs where the minor groove is narrow and 2) DNA kinks, which are caused by the unstacking of a single base pair.

Base readout: One ingrained way for proteins to achieve DNA binding specificity is through contacts with the bases in either the major or minor groove that recognize the chemical signature of the base or base pair. This type of recognition is generally mediated by the formation of hydrogen bonds between amino acids and bases, which convey the highest degree of specificity, and, in some cases, by water-mediated hydrogen bonds, o hydrophobic contacts.

Base-specific interactions in the major groove: Hydrogen bonds with bases can confer greater specificity in the major groove than in the minor groove because the four possible base pairs have a unique pattern of hydrogen bond donors and acceptors in the major but not in the minor groove. Proteins that form hydrogen bonds with bases in the major groove use HTH domains (e.g., homeodomains, λ repressor, Trp repressor).

Base-specific interactions in the minor groove: Proteins can also form hydrogen bonds with bases in the minor groove, although, the pattern of donors and acceptors in the minor groove does not distinguish AT from TA or GC from CG base pairs. Some proteins, High mobility group (HMG) proteins form hydrogen bonds in the minor groove but rely on the recognition of DNA shape and flexibility.

Goals for this review: We simply summarize the major protein super familes that are observed in DNA binding proteins. Second, because interactions between proteins and DNA depend on the interplay between both macromolecules, we review the range of interactions that are observed at protein-DNA interfaces, our goal is to present a richer and more subtle view of protein-DNA recognition that more accurately reflects the way in which evolution has fine-tuned these essential interactions.

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Antiulcer potential of *Qusqualis indica* leaves in experimental animals

Mayank Kulshreshtha*[1], Manjul Pratap Singh

[1]Ph.D Research Scholar, Department of Pharmacology, School of Pharmacy, Babu Banarsi Das University, Lucknow, India

[2]Sr. Assistant Professor, Department of Pharmaceutics, School of Pharmacy, Babu Banarsi Das University, Lucknow, India

E.mail: professormayank@gmail.com

ABSTRACT

Quisqualis indica Linn (*Q.indica*), family- Combretecea, vining and evergreen plant, broadly grown in India as ornamental plant in most of the gardens. Traditionally different parts of this plant have different uses like root, seed and fruit can be used as kill parasitic worms. Fruit can also be used for nephritis. Leaves can be used to relieve pain whereas roots are used to treat rheumatism. Pharmacologically *Q.indica* have anti-inflammatory activity, Immunomodulatory Activity, Anti-staphylococcal Activity, as a acetylcholinesterase Inhibitor etc. The present study investigated the antiulcer potential of different extracts of *Quaqualis indica* leaves against different models. To explore the potential of different extracts, different models used like pylorus ligation, ethanol induced ulcers, stress induced ulcer. The animals dived into six groups such as Group 1 served as a negative control group which treated with inducers (Pylorus ligation/ ethanol/ stress).Group 2 served as a standard group which treated with Sucralfate (250 mg/kg). Group 3 served as test group 1 which treated with AEQI (200 mg/kg). Group 4 served as test group 2 which treated with AEQI (400 mg/kg). Group 5 served as test group 3 which treated with EEQI (200 mg/kg). Group 6 served as test group 4 which treated with EEQI (400 mg/kg). Different leaf extracts were treated with different reagent for the presence and absence of various secondary metabolites. Phytochemical analysis of different extracts showed the presence of different secondary metabolite like alkaloids, glycosides, tannin, saponin, phenolic compounds etc. In case of Pylorus ligation method, pyloric end of stomach tied by the help of suture so that accumulation of acid will be take place and mucosal damage due to excess of acid or it is shown by auto digestion of mucosa and decrease

of mucosal barrier. In pylorus ligation method, AEQI (400 mg/kg) found to be significantly effective that gave 77.03% protection against PU while EEQI at the same dose found to be effective that is 76.29% compared to negative control group. Both of the extracts have antiulcer property within a dose dependent manner. The same thing repeated in another two models. The plant *Quaqualis indica* has a antiulcer property in a dose dependent manner.

Key words: *Quaqualis indica,* antiulcer, pylorus ligation.

Renin-angiotensin-aldosterone system (RAAS) pathway gene polymorphisms are associated with High altitude pulmonary edema (HAPE) sensitivity

Shuchi Bhagi[1*] and Shashi Bala Singh[2]**

[1]Institute of Nuclear Medicine and Allied Sciences (INMAS), Brig. SK Mazumdar Marg, Timarpur, Delhi-110054

[2]O/o Director General (Life Sciences), DRDO Bhawan, Rajaji Marg, Vijay Chowk Area, Central Secretariat, New Delhi, Delhi 110004

*Presenting Author Email: shuchi_1112@yahoo.co.in **Corresponding Author Email: drshashisingh@gmail.com

ABSTRACT

High altitude pulmonary edema (HAPE) is a life threatening condition affecting non-acclimatized individuals who ascend rapidly to high altitude (HA) (elevation >2,500m) within 2-5 days of arrival and is a cause of most of the deaths due to high-altitude illnesses. Studies have indicated that genetic variability is a key factor in making a person susceptible or acclimatized to HAPE. Studies have shown a possible association between the gene polymorphisms of renin-angiotensin-aldosterone system (RAAS) pathway in regulation of vascular tone circulatory homeostasis and might play a role in individual sensitivity towards HAPE, forming the basis of this study. To understand the genetic basis of HAPE targeting at RAAS pathway candidate genes as potential risk predictors of altitude susceptibility. A total of 223 Indian Army volunteers (119 HAPE patients and 104 acclimatized controls) were recruited for the study. Genetic variants were studied in seven relevant *SNPs* and *Ins/Del* occurring in five candidate genes of RAAS pathway: *(-4063)C>T* (rs41317140) and *A/G*$^{i8\text{-}83}$ (rs2368564) of Renin *(REN); M(235)T* (rs699) of Angiotensinogen (*AGT); I/D* (rs1799752) Angiotensin-Converting Enzyme (*ACE); 1166A>C* (rs5186) and *A-777T* (rs275651) *of* Angiotensin Receptor *(AGTR1)* gene and *CYP11B2 T>C(-344)* (rs1799998) *SNP of* Aldosterone Synthase genes were analyzed using PCR-RFLP genotyping followed by statistical analysis. Two SNPs viz. *AGTR1 1166A>C*, *CYP11B2 T>C (-344)* and one insertion-deletion variant *ACE I/D* (rs1799752) exhibited a statistically significant difference at both genotypic and allelic levels between the two groups. In *AGTR1 1166A>C SNP* the dominant genotype *AA* was significantly predominant in patients as compared to controls. In *CYP11B2 T>C (-344),* the wild type *-344T* allele which provides benefit to HA population is the at-risk allele for the sea level population in Indian subjects. *ACE* gene showed an *I*-allele performance benefit is seen at the extreme HA conditions, making it an advantageous loci and *D* allele as the at-risk allele for HAPE susceptibility. The genotypes favoring increased activity of RAAS were higher in HAPE patients compared to resistant controls, suggesting overall activation of RAAS pathway and its contribution to pathogenesis of HAPE.

Keywords: High Altitude Pulmonary Edema, Renin-Angiotensin-Aldosterone System, Single Nucleotide Polymorphisms

Unveiling the Pleiotropy of Leukemia Inhibitory Factor (LIF) through to and fro Mass Spectrometry and Protein Chemistry approach

Syed Azmal Ali[#], Ashok Kumar Mohanty, Sudarshan Kumar*

Proteomics and Cell Biology Lab, Animal Biotechnology Center,

National Dairy Research Institute, Haryana, India , *Email:* azmal786@gmail.com; kumarsudershan@gmail.com

ABSTRACT

Leukemia inhibitory factor (LIF) is a polyfunctional cytokine belongs to an IL-6 class of interleukin family. It's presence in various organs are ubiquitous, but the vital pathways induced by LIF for cell survival and polarity is scantily implicated. We over expressed the LIF in COS-1 cells and purified using affinity chromatography and confirmed via MS/MS. The purified LIF was verified for its functional activity by different assays such as BrdU, MTT, migration, Caspase 3/7, western and RT-qPCR. Further, we have applied high-resolution LC-MS/MS based LFQ

approach for the identification DEGs (Differentially Expressed Proteins) and deep bioinformatics analysis for 5 common PTMs cross talk on Cytoscape platform. **T**he MW of LIF with and without glycosylation is 58.99 kDa and 48.9 kDa respectively was determined. The purified LIF showed maximum inhibition at 72 hours and half-maximal effective concentration (EC50) of 0.0555 ng/mL, corresponding to a specific activity of $>1.6\times10^7$ units/mg and identified IC50 value for migrating cells to be 77.8ng/ml. The MS/MS data identified 2083 proteins in DDA mode with the overall PSM as 16032. We further validated the MS data using RT-qPCR and western blot. Subsequently, elucidate the LIF-mediated cascade for activation of MEK/ERK, Ras, mTOR, Hippo, and RAP1 pathways. Finally, we conclude that LIF involves in autocrine-paracrine mediated cell cycle signaling. These identified targets suggest that LIF could be an important prognostic marker for various diseases such as neurodegenerative diseases and cancer.

Keywords: Leukemia Inhibitory Factor; Cytokine, Pathways, Mass Spectrometer

Association of Angiotensin II Type 1 Receptor A1166C Gene Polymorphism with Hypertension in Chronic Kidney Disease Patients of Uttar Pradesh

Narendra Mohan Verma, Sanjeev Kumar Maurya
Department of Biotechnology, Invertis University, Bareilly, Uttar Pradesh-243123, India
E-mail: narendra_106@yahoo.com

ABSTRACT

Angiotensin II type 1 receptor (AGTR1) plays an important role in the development of hypertension and progression of renal disease to chronic kidney disease (CKD). Hypertension is also a strong risk factor for the development CKD. The aim of this study is to investigate the association of *AGTR*1 A1166C with hypertension in patients of CKD among Uttar Pradesh population. This study included unrelated 121 CKD patients (66 patients with hypertension and 55 patients without hypertension) and 44 healthy controls. Genotyping was carried out by PCR-RFLP method. A statistical significance was found in the genotypes of *AGTR*1 A1166C between CKD patients and controls. Further studies are needed to ascertain the tight relationships of *AGTR*1 A1166C gene polymorphism with CKD of different etiologies

Protein profiling of *Pseudomonas fluorescens* lytic Bacteriophages isolated from BHS infected fishes of sub Himalayan region

Nisha Dinkar, Suneeta Gangwar, Ruchi Mishra, Nisha Kumari, Ankur kashyap and Yogendra Prasad
Khandelwal College of Management Science and Technology
Department of Animal Science, M.J.P. Rohilkhand University, Bareilly-243006 (U.P.)

ABSTRACT

This investigation was aimed to develop antibacterial strategy to circumvent the problem of antibiotic resistant infecting *Labeo rohita* and Indian walking catfish, *C. batrachus* in Himalayan and Sub Himalayan regions. Four lytic phages (PFPD, PFPK, PFPN and PFPC) were isolated against ten isolates of *P. fluorescens* following overlay method using water and bottom sediments of Himalayan and Sub Himalayan regions. One step growth experiment was carried out to know the eclipse, latent periods and burst size of phages. Isolation of phage protein was made as per Laemmli (1970) with slight modification. Phages were identified as a member of *Siphoviridae* family with having structural viral proteins of 22 - 102 kDa. Phages exhibited minimum eclipse period (10 - 15 min), latent period (20 min) and highest burst size of 130. These phages conferred clear lytic plaques in the lawn of 8 of 10 (80%) host bacterium at 0.01 MOI. The profound lytic attributes of PFPD and PFPK phages with aquaculture activities reveals that they may be a suitable option to alleviate transmission of even systematic infection in hatchery and culture system. This information will provide more insight into the potential use of phage to mitigate incidences of Bacterial Haemorrhagic Septicaemia in aquaculture.

Keywords: *P. fluorescens, L. rohita, C. batrachus.*

Physico-chemical and Mineral content study of Some Selected Medicinal Plants of Family Apocynaceae

Anuj Kumar Sharma, Ruchi Mishra, Shalini Gupta
Department of Chemistry, Khandelwal College of Management Science and Technology, Bareilly *anujkumarsharma077@gmail.com

ABSTRACT

In current drug discovery physico-chemical analysis and mineral content studies are also playing an important role. In present study we have selected *Wrightia tinctoria*, *Wrightia coccinea*, *Wrightia mollissima* and *Wrightia tomentosa* of family Apocynaceae. There is a relationship between the element content of the plant and its nutritional status. Four medicinal plants species of *Wrightia* were authenticated by Prof. S.K. Upadhyaya, Department of Botany, M.S. College, Saharanpur and were was collected from Government garden Saharanpur U.P. also from Shivalik hills. In present study we have studied the extractives, total ash and acid insoluble ash contents, mineral contents. The followed procedure is given in IP (1996). Chloroform solvent gives maximum yield in *Wrightia coccinea.* Alcohol solvent gives maximum yield in *Wrightia tinctoria* and water solvent gives maximum yield in *Wrightia mollissima.* Total ash, acid insoluble ash, water soluble ash and Water, Alcohol Soluble Extractives were also maximum in *Wrightia mollissima* wheres as *Ca* was maximum in *Wrightia tinctoria*. Fe was maximum in *Wrightia coccinea* and Cu was maximum in *Wrightia mollissima.* The results confirm that all these plants may be a good source of minerals and extractive values to treat number of diseases.

Keywords: Mineral analysis, medicinal plants, physico chemical

Synthesis and characterization of Copper(II), Nickel(II), Cobalt(II), Zinc(II), Tin(IV) and Cadmium(II) complexes as potent anticancer agents

Shalini Gupta*, Ruchi Mishra, Anuj Sharma
Department of Chemistry, *Khandelwal College of Management Science and Technology,* Bareilly, *shalinidr74@gmail.com

ABSTRACT

The Kinetic Knowledge of the interaction of such metal complexes with DNA fragment Vis-à-vis sulpher containing biomalecule of importance in rationalization of the antitumor activity as well as toxicity of such metallo drugs. Here we report Ferrounyl phenyl-N-Thisemicarbazone legends HFptsc, HAfptsc and their complexes with some metal and organization ions. The compounds Me_2SnCl_2 and $MeSnCl_3$ were prepared (Luisten and Vandu kirk) while Me_3Sic=Cph and the ferrocene derivatives was prepared as described in literature. A few complex of copper(II), Nickle(II), Cobalt(II), Zinc(II), Tin(IV) and cadmium(II) with two synthesized organ metallic compound, Formylferrocene Phenyl-N-thiosemicarbazone (HFfptsc), 1-acetyl ferrocene phenyl N-Me_2SnCl_2 and thiosemicarbazone (HAfptsc) have been isolated. The intuaction of (HFfptsc) with Me_2SnCl_2 and Me_2SnCl_3 yield a series at organotin(IV) compounds. These complexes have been characterized on the basis of elemental analysis, molecular weights, molar conductances, magnetic moments and spectroscopic data. The results are very valuable because various complexes have been synthesized and characterized having anticancer activity.

Keywords: anticancer agents, metal complexes, spectroscopic analysis

Discovery of potent *Toxoplasma gondii* DHFR inhibitors through pharmacophore modeling and virtual screening

Ruchi Mishra[1]*, Shalini Gupta[1], Anuj Sharma[1], Nisha Dinkar[1], Sarvesh Paliwal[2]
[1]Khandelwal College of Management Science and Technology, *Bareilly*
[2]Banasthali University, Rajasthan, **drrmishra39@rediffmail.com*

ABSTRACT

Toxoplasma gondii, the causal agent of toxoplasmosis, is an important water and food borne protozoan parasite. Due to various problems associated with tgDHFR inhibitors there is great interest in developing potent and selective tgDHFR inhibitors. A ligand-based pharmacophore model using Catalyst-HypoGen algorithm was developed for set of aminopteridine, dezapteridine and quinazoline analogues as tgDHFR

inhibitors.The best pharmacophore model for selective tgDHFR inhibitors (Hypo-1) was obtained through a Cat-Scramble validation process which consisting of one hydrogen bond acceptor-lipid (HBAl), two hydrophobic (HY) and one ring aromatic (RA) features, with highest correlation coefficient (0.89), cost difference (75.09), low RMS (0.94) with a high fit and predictive power. Model was validated toward a test set (22) and also through external test set. Through screening chemical data base (Mini Maybridge and NCI) eight druggable leads were identified. The results of our study will act as a valuable tool for retrieving potent compounds with desired biological activities and designing novel selective tgDHFR inhibitors.

Keywords: tgDHFR, Pharmacophore, virtual screening

Investigation of ZnO, MWCNT and MSN Nanomaterials effect on *in vivo* and *in vitro* for Nano-safety assessment via quantitative proteomic approach

Karmveer Yadav and Gautam Kaul*
Division of Animal Biochemistry, ICAR-NDRI, Karnal, 132001, India.
*Corresponding author. Tel: (0184) 2259132; Fax: (0184) 2259132;
E-mail: gkndri@gmail.com

ABSTRACT

Nanotechnology have immense application in various fields, Nanomaterials (NMs) usage is increasing day by day. However, without a comprehensive assessment of their properties and associated effects, these cannot be marked as completely safe. In this context, it becomes relevant to realize their cytocompatibility, adverse effects and experimental evaluation by *in vivo* and *in vitro* testing with various cell lines and animal models. Healthy female rat expose daily to MSN, MWCNT and ZnO NPs. Ovarian tissue samples were collected after 14 days and were analysed using iTRAQ-based quantitative proteomics approach. Similarly, for in vitro analysis CHO-K1 (2 x10^5) cells were seeded on 96-well plate. After 24 h stabilization cells were exposed to the increasing NMs concentration for 24 h. At the end of exposure, cell viability (MTT and Neutral Red assay) of the treated group was calculated as a percentage of non-treated control cells.The results showed that decrease in ovary size and follicles count were the prime malformations induced by ZnO and MWCNT NMs. The level of Estrogen and Progesterone were found to decrease as compared to control. CYP450 reductase activity was decreased significantly by ZnO and MWCNT. Further cell line treated for short-term exposure (3-24h) showed decrease in viability with increasing concentration. Additionally, our *in vitro* proteome profiling data revealed more than 7000 protein which is importance to cellular and molecular function of cell. In regard to the sensitivity of the assays performed, NRU assay appeared to be less sensitive as compared to MTT in detecting cell viability upon exposure to ZnO.

Keywords: Proteomic; CHO-K1 cell line; Ovary

Utilizing α-Amylase As A Template To Design Novel Anti-biofilm Peptide Molecules

Shivam Mishra, Vishal Srivastava,and Tapan Kumar Chaudhuri*
Kusuma School of Biological Sciences, Indian Institute of Technology Delhi, Hauz Khas, New Delhi, India, *Email:* microbiologistshivam@gmail.com

ABSTRACT

Biofilm is a union of microorganisms in which microbial cells adhere to each other on living or non-living surfaces within a self-produced matrix of extracellular polymeric substance (EPS). Bacterial biofilm is infectious in nature and can result in nosocomial infections or hospital-acquiredinfections. Alpha amylase is a natural anti-biofilm agentfound in *Aspergillus oryzae*, *Bacillus subtilis*, and human saliva. Alpha amylase is involved in degrading the biofilm matrix permitting increased penetration of antibiotics. Alpha amylase is a proven antibiofilm agent against *S. aureus*(MRSA*)*, *vibriocholerae* and *pseudomonasaeruginosa* in not only inhibiting biofilm formation but also in degrading preformed mature biofilm. Our aim is to design a novel anti-biofilm peptide molecules utilising alpha amylase enzyme as a template which will be effective in inhibting biofilm formation.According to our hypothesis,approximately 70-90 %inhibition will beprovided by thenew template of alpha amylasein particular species.

Keywords: Biofilm, extracellular polymeric substance, α-amylase, nosocomial infections

Prediction of Hn And Slam Protein Interaction And Synthesis of Antiviral Agents Against Ppr Virus

Aditya Agrawal*, P. Kirthika, Anil Gattani, Praveen Singh[1]
Division of Animal Biochemistry, IVRI Bareilly-243122
1. Principal Scientist, CIF- Bioengineering and Biophysics Section, IVRI, Bareilly- 243122
* corresponding Author: Email: agrawaladitya1986@gmail.com

ABSTRACT

Peste des petits ruminants (PPR) also known as 'goat plague' is considered as one of the most dreadful disease of small ruminants having morbidity rate of 90% and mortality rate of 50–80% in susceptible populations. PPR is emerging in new regions of the world and is causing great economic losses, threatens the food security and sustainable livelihood of farmers across Africa, the Middle East and Asia. The entry of virus particles in the cell requires specific interactions between host cell receptors and viral encoded capsid proteins. Molecular predictions of virus protein and host cell receptor interactions may help in adopting different strategies to design and develop novel antiviral agents to fight infections. Molecular decoys, one among the various approaches against viruses, are agents specifically resembled synthetic peptides mimicking the binding domain of the receptors. Recently it has been reviewed that SLAM (signaling lymphocyte activation molecules) or CDw150, appears as the surface receptor for the PPR virus HN protein to get entry inside the cell. SLAM/CDw150 FASTA sequence was retrieved out from NCBI site (https://www.ncbi.nlm.nih.gov/protein/XP_002760222.1?report) and using antigenic determinants software the antigenic region on SLAM which able to bind to NH/H protein of PPR Virus was find out (http://imed.med.ucm.es/Tools/antigenic.pl). A series of short amino acid stretch of 15-22 sequences from the SLAM/CDw150 has been predicted out, which have the high affinity score against the HN/H protein of PPR virus. The predicted peptide has been synthesized by solid phase peptide synthesis (SPPS), using F-moc chemistry and purified by HPLC. The synthetic peptide is conjugated with Gold Nanoparticles (GNP's) and their interaction with the PPR virus has been visualized and characterized by different spectroscopic methods.

Efforts to Reduce Greenhouse Gases, Air Pollution and Climate Change: Global and Regional Perspectives

Anil Patel, Shraddha Rawat
Department of Meterology SHUATS Naini, Allahabad, India
E-mail : anilpatelkwd88@gmail.com

ABSTRACT

Greenhouse gases (GHGs) warm the surface and the atmosphere with significant implications for rainfall, retreat of glaciers and sea ice, sea level, among other factors. About 30 years ago, it was recognized that the increase in tropospheric ozone from air pollution (NO_2, CO_2 and others) is an important greenhouse forcing term. In addition, the recognition of chlorofluorocarbons (CFCs) on stratospheric ozone and its climate effects linked chemistry and climate strongly. The major sources of this air pollution include fossil fuel combustion for power generation and transportation; cooking with solid fuels; and burning of forests and savannah. The ultimate by-product of all forms of burning is the emission of the colorless gas, carbon dioxide (CO_2). Since CO_2 does not react with other gases in the atmosphere, the greenhouse effect was largely a problem of solving the physics, thermodynamics and dynamics of climate. The independent discoveries of the CFC effect on stratospheric ozone chemistry and on the greenhouse effect, coupled atmospheric chemistry strongly with climate. The reduced long wave radiation from the cooler stratosphere and the reduction on ozone greenhouse effect dominated the solar effect. Thus climate and air chemistry became strongly linked. One point to noted is that the predicted warming of 2.4^{0}C is the equilibrium warming, which is basically the warming we will observe decades to century from now, based on the buildup of greenhouse gases since the dawn of the industrial era, we have committed (the planet to a warming of 2.4^{0}C. About 0.6 ^{0}C of the observed warming can be attributed to the GHGs forcing and about 0.5 ^{0}C is stored in the oceans. The stage is set now to consider the masking effect of aerosols. To underline their air pollution origin, we refer to the aerosols as atmospheric brown clouds (ABCs) 1) The primary conclusion is that without a proper treatment of the regional and global effects of ABCs in climate models, it is nearly impossible to reliably interpret or understand the causal factors for regional as well as global climate changes during the last century By improving the living conditions of the rural poor (average earning is less than 2 $ a day) and by minimizing the negative health impacts of indoor smoke, for solving the air pollution and global warming problem. Replacing solid fuel cooking with other alternative clean energy sources such as solar and biogas plants may seem promising, thus efforts to reduce (GHGs) and air pollution should be done under one common framework. The uncertainties in our understanding of the (ABCs) effects are large, but we are discovering new ways in which human activities are changing the climate and the environment.

Keywords: Greenhouse gases, CFC, Aerosols, Global warming.

Adiponectin: A Potential Biomarker for Alzheimer's disease

Arpit Dixit, Tarun Upadhyay, Raj Vardhan Tripathi, Mohammad Mustufa Khan*
Department of Life Science, Institute of Applied Medicine and Research, Delhi-Meerut road, Ghaziabd (U.P)-201206
*Email Id: dixitarpit71@gmail.com, mohammad.mustufa@iamr.ac.in

ABSTRACT

Adiponectin is a protein hormone and an adipocytokine released by the adipose tissue. It circulates as trimers, hexamers, and a high molecular weight form. Adiponectin acts by binding to its receptors, adiponectin receptor type 1 and type 2. Adiponectin receptors are expressed in skeletal muscle, liver, hypothalamus and vascular endothelial cells of brain. Adiponectin has important roles in the metabolic syndromes such as obesity, cardiovascular disease, type 2 diabetes (T2DM) and also neurodegenerative disorders. Adiponectin modulates brain metabolism and sensitivity of insulin regulating memory and cognitive dysfunction and it also regulates severe inflammaion observed in mild cognitive impairment and Alzheimer's disease (AD). In particular, adiponectin contributes to the deregulated glucose metabolism and mitochondrial dysfunction observed in AD. Specifically, adiponectin increase in blood insulin, not glucose level in AD. Insulin dysregulation contribute to AD pathologies by several mechanisms from reduced brain gulcose utilization to neurofibrillary tangle formation and increased amyloid β aggregation by insulin degrading enzyme inhibition. Insulin affects neuronal cognition and memory through several levels by regulating ion channels, neurotransmitter receptors and synaptic transmission in AD brain. Amyloid β accumulation induces the oxidative stress and mitochondrial dysfunction, and these dysfunctions induces AD pathogenesis. Adiponectin is protective against amyloid β neurotoxicity in AD. Adiponectin modulates amyloid β in AD and so improves cognition. Various studies demonstrate that the insulin sensitizing action of adiponectin may be another mechanism of neuroprotection in AD. Hypoadiponectinemia in the brain may be implicated in neurodegeneration during aging. The reduced adiponectin levels in T2DM patients may be a factor which increases the risk of AD. Thus, adiponectin may be a promising therapeutic target to alleviate AD pathologies such as apoptosis and cognitive decline and dysfunctional brain insulin system.

Keywords: Adiponectin, Adiponectin receptors, Alzheimer's disease, Type 2 Diabetes Mellitus

Exploration of matrix metalloproteinases association with Osteoarthritis

Chandra Shekhar Azad[1], Manish Singh[2], Manish Tripathi[3], Alok Kumar Singh[1], Indrajeet Singh Gambhir[1]
[1]Department of Medicine, Faculty of Medicine, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India 221005
[2]Department of Pharmacology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India 221005
[3]Department of Pharmaceutical Engineering, Indian Institute of Medical Sciences, Banaras Hindu University, Varanasi, India 221005

ABSTRACT

Osteoarthritis (OA) is the ubiquitous form of chronic joint disorder occurs due to breakdown of articular cartilage and cause pain and stiffness in joint, swelling, muscle weakness, and joint instability leads to gradual loss of physical function of body and pitiable quality of life. Matrix Metalloproteinases (MMPs) are a family of zinc and calcium-dependent proteolytic enzymes which digest various components of extracellular matrix (ECM), including collagen, laminin, fibronectin, vitronectin, elastin and proteoglycans of diverse physiological and pathological processes. The activity of MMPs is regulated at multiple levels. MMPs are categorized into several groups on the basis of their structure and function. The aim of this study was to examine the role of different MMPs in osteoarthritis and its complications. Bioinformatics analysis of several MMPs were done in this study and found that the MMPs are connected with several signaling mechanism related to the complicated diseases and considerably involve in inflammatory joint disease. During this intervention of analysis, MMPs are also found to behave as connecting link between many chronological diseases.

Polymeric nanoparticle-encapsulated curcumin (Nanocurcumin): A novel strategy for cancer therapy

Gunjan Raghav, Vershanjali Solanki
Department of Life Science, Institute of Applied Medicine and Research, Ghaziabad, E mail: versha.solanki27051994@gmail.com

ABSTRACT

Curcumin, a yellow polyphenolic compound extracted from the rhizome of turmeric (*Curcuma longa*) which has potent anti-cancer properties as demonstrated in a plethora of human cancer cell line and animal carcinogenesis models. Nevertheless, it is widely used in clinical application of cancer and other diseases where it has been limited due to poor aqueous solubility and consequently minimal systemic bioavailability. Nano-particle-based drug delivery approaches have the potential for rendering hydrophobic agents like curcumin dispersible in aqueous media, thus circumventing the drawback of poor solubility. Therefore, polymeric nano-particle encapsulated formulation of curcumin was developed utilizing the micellar aggregates of cross-linked and random copolymers of Nisopropylacrylamide (NIPAAM) with N-vinyl-2-pyrrolidone (VP) and poly(ethyleneglycol)monoacrylate (PEG-A). Physico-chemical characterization of the polymericnano-particles by dynamic laser light scattering and transmission electron microscopy confirms an arrow size distribution in the 50 nm range. Nanocurcumin, unlike free curcumin is readily dispersed in aqueous media. Nanocurcumin demonstrates comparable *in vitro* therapeutic efficacy to free curcumin against a panel of human pancreatic cancer cell lines, as assessed by cell viability and clonogenicity assays in soft agar. Further, nano-curcumin mechanisms of action on pancreatic cancer cells is similar that of free curcumin including induction of cellular apoptosis, blockade of nuclear factor kappa B (NFκB) activation, and down-regulation of steady state levels of multiple pro-inflammatory cytokines (IL-6, IL-8, and TNFα). Therefore, nano-curcumin provides an opportunity to expand the clinical range of this efficacious agent by enabling ready aqueous dispersion. Future studies utilizing nano-curcumin are warranted in pre-clinical *in vivo* models of cancer and other diseases that might benefit from the effects of curcumin.

Keywords: Curcumin, Nisopropylacrylamide, Clonogenicity.

Molecular Genetic analysis on Angiotensin-converting enzyme (*ACE*) gene insertion/deletion (I/D) polymorphism in hypertensive patients of North India

Mritunjai Singh, Alok Kumar Singh, Poorti Pandey, Subhash Chandra, Chandra Shekhar Azad, Indrajeet Singh Gambhir
Department of Medicine, Institute of Medical Sciences, Banaras Hindu University, Varanasi
E-mail: mritunjai.singh@gmail.com

ABSTRACT

Angiotensin-converting enzyme (ACE) is the key enzyme of the renin angiotensin system (RAS) which maintains the blood pressure homeostasis and fluid and salt balance. The association of the ACE insertion/deletion (I/D) polymorphism with essential hypertension has been demonstrated by many earlier studies. The purpose of the present study is to investigate the insertion/deletion polymorphism of the ACE gene and its association with hypertension and additive diseases like diabetes and cardiovascular diseases in north Indian population. Total, 440 subjects were analysed including 222 hypertensive and 218 normotensive. Anthropometric measures, lipids profiles, blood glucose, and blood pressure (BP) measures were collected from participants. *ACE* I/D polymorphism was determined by using insertion-specific amplification. Significant differences were observed in the frequencies of DD, ID, and II genotypes among the hypertensive and normotensive groups which were found to be 29.7%, 38.7%, and 31.6% vs. 53.7%, 23.4%, and 22.9%, respectively. It has been observed that the *ACE* ID genotype was significantly ($p < 0.05$) higher in hypertensive subjects, whereas, the DD genotype was significantly ($p < 0.05$) higher in normotensive subjects. A strong association was found between cardiovascular diseases (CVDs) and ID genotype [$p = 0.017$, odds ratio (OR) = 3.091, 95% confidence interval (CI) = 1.224–7.807]. ID [$p = 0.002$, OR = 2.020, 95% CI = 1.281–3.185] and II [$p = 0.032$, OR = 1.677, 95%CI = 1.044–2.694] genotypes are more susceptible to diabetes with hypertension. These findings suggest that *ACE* insertion/deletion polymorphisms are associated with hypertension and additive diseases in North Indians.

Approach of NGS in assembling genome of Bacteriophage

Raja Ishaq Nabi Khan*, Waseem Akram Malla and Sheikh Firdous Ahmad
ICAR-Indian Veterinary Research Institute, Izatnagar 243 122, Bareilly (UP), India., Corresponding author: ishaaq.raja@gmail.com

ABSTRACT

The dawn of next generation sequencing technologies has opened up exciting possibilities for whole genome sequencing of a plethora of organisms. The 2nd and 3rd generation sequencing technologies, based on cloning-free, massively parallel sequencing, have enabled the generation of a deluge of genomic sequences of both prokaryotic and eukaryotic origin in the last decade. However, whole genome sequencing of bacterial viruses has not kept pace with this revolution, despite the fact that their genomes are orders of magnitude smaller in size compared with bacteria and other organisms. Sequencing phage genomes pose several challenges; (1) obtaining pure phage genomic material, (2) PCR amplification biases and (3) complex nature of their genetic material due to features such as methylated bases and repeats that are inherently difficult to sequence and assemble. Using Sanger, 454, Illumina and PacBio technologies, sequencing runs can easily add up to several hundred gigabases of raw sequence and large assemblies. A reliable and redundant data storage option is mandatory to ensure data safety and consistency. However, not all bacteriophage genomes sequence effortlessly and potential obstacles to sequencing, such as DNA structure, sequence repeats and problems due to DNA methylation, particularly of epigenetics, must be taken into account. A blended approach of a long-read technology is proposed for scaffolding purposes combined with a large number of short reads from a second technology for efficient DNA sequencing of bacteriophage genome.

A Phenomena: Protein Folding To Misfolding

Shamshul Huda[*]; Dr. Nitesh Kumar Poddar[1]
[*]DR. B.R. Ambedkar Center for Biomedical Research, North Campus, 110007 University of Delhi, INDIA.
[*]Saint. Jeelani Public School Sambhal 244302, INDIA.
[1]Department of Biotechnology, Invertis University, Bareilly, INDIA.
E-mail: shamsultech@hotmail.com;

ABSTRACT

A living organism may contain as many as 100000 different types of protein. For a protein to function appropriately, it must first achieve its proper conformation and location within the crowded environment inside the cell. In eukaryotic cells, the endoplasmic reticulum is essential for the folding and trafficking of proteins that enter the secretory pathway. Multiple chaperone systems are required to fold proteins correctly. Environmental insults or increased protein synthesis often lead to protein misfolding in the organelle, the accumulation of misfolded or unfolded proteins known as endoplasmic reticulum stress and the activation of adaptive unfolded protein response to restore homeostasis. If protein misfolding is not resolved, cells die. Endoplasmic reticulum stress and activation of the unfolded protein response help to determine cell fate and function. Furthermore, endoplasmic reticulum stress contributes to the aetiology of many human diseases. Protein misfolding in the ER causes accumulation of misfolded proteins (ER stress) and activation of the unfolded protein response (UPR), which has evolved to maintain a productive ER protein-folding environment. Both ER stress and UPR activation are documented in many different human cancers.

Over expression of Tumour Associated Antigens (TAA) during cancer

Shumaila Khan, Sonal Saxena, Poonam Singh
Animal Biotecnology Department,IVRI Bareilly (U. P.) India.
Department of Molecular and Cellular Biology,SHUATS Allahabad (U.P) India, shumaila6@gmail.com

ABSTRACT

Mammary gland tumors are the most frequently encountered group of neoplasms in Canine. Mammary tumors can be benign (noncancerous) or malignant (cancerous) and can arise from different types of tissues (epithelial, glandular, mesenchymal or connective tissue) in the mammary gland. The most common types are tumors from the glandular tissues and include adenoma, carcinoma, and adenocarcinoma. The risk

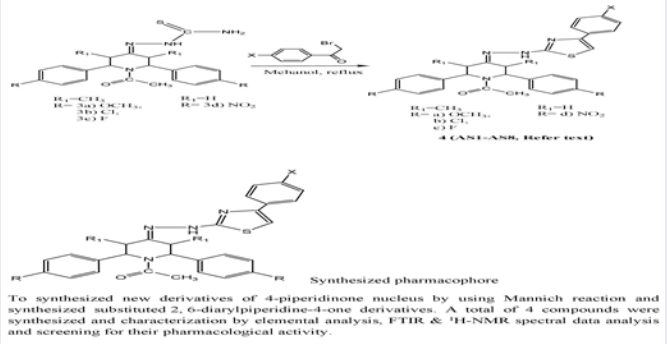
of developing mammary gland tumors is closely associated with exposure to the female sex hormones, estrogen, and progesterone, in early years of development. The hormones may also provide continuous stimulation to tumors and contribute to tumor progression. Mammary tumors over-express certain Tumour Associated Antigens (TAA), which can be diagnosed at very early stage of a mammary tumour. TAAs can be used as markers against Canine Mammary Tumours (CMTs) and also can be used for development of various assays for diagnosis of mammary cancer at an early stage both in dogs and humans. The identification of antigens that are over-expressed in Canine Mammary Tumour which would help in the early prognosis of mammary tumors in bitches and human females in future.

Synthesis, Structure Elucidation and Characterization of novel substituted 2, 6-diarylpiperidine-4-one derivatives

Himanshu Joshi
Invertis Institute of Pharmacy, Invertis University, Bareilly, Uttar Pradesh, India.
Correspondence Author- hijoshi1234@gmail.com, himanshu.j@invertis.org

ABSTRACT

Today medicinal chemistry is offering many complicated challenges. The most difficult and at the sometime most rewarding challenge is the rational design of new therapeutic agents for treating human disease. Piperidione serve as important role as intermediate of substituted piperidine and they are found to be part of more complex biologically active compound apart from analgesic, anti inflammatory, anti fungal, local anaesthetic and antihistamine are valuable synthetic intermediate for the preparation of various alkaloid and pharmaceutical compound. This prompted to me, to synthesized new derivatives of 4-piperidinone nucleus by using mannich reaction and synthesized substituted 2, 6-diarylpiperidine-4-one derivatives. A total of 8 compounds were synthesized and characterization by elemental analysis, FTIR & ^{1}H-NMR spectral data analysis.



To synthesized new derivatives of 4-piperidinone nucleus by using Mannich reaction and synthesized substituted 2, 6-diarylpiperidine-4-one derivatives. A total of 4 compounds were synthesized and characterization by elemental analysis, FTIR & ^{1}H-NMR spectral data analysis and screening for their pharmacological activity.

Keywords: Piperidione, Anti Inflammatory, Antihistamine, Mannich reaction, 2,6 diarylpiperidine-4-one.

In vitro Antioxidant Activity of *Acacia Arabica*

Vershanjali Solanki, Gunjan Raghav
Department of Life Science, Institute of Applied Medicines and Research, Ghaziabad
E mail: versha.solanki270594@gmail.com

ABSTRACT

The two extraction methods were evaluated on free radical scavenging activity. Extraction is done on same plant, i.e., *Acacia Arabica*. Results indicated that the sequential extraction method was effective in concentrating the active principles in the ethanol extract as compared to the maceration method in DPPH assay. Ethanol extract rich in phenolic and flavonoid contents had potent antioxidant activity. The possible antioxidant mechanism of the ethanol extract can be due to its hydrogen or electron donating and direct free radical scavenging properties. The bark powder of the plant *Acacia Arabica (*L.*)* Wild. Extracted with different solvents of increasing and decreasing polarity by maceration extraction method. The scavenging activity in lipid peroxidation assay and results were compared with standard antioxidants (butylated hydroxytoluene). The activity of extract was found to increase on fractionating the extract. The antioxidative activites, including the 12-12 diphenylpicryl-hydrazyl (DPPH) radical-scavenging effects, hydroxyl radical scavenging potential, chelating ability, reducing power and lipid inhibition in vitro and were more effective. A polyphenolic compound has been isolated from methanol extract of *Acacia Arabica* Wild.

All the bark extracts exhibited wide range of total phenolic, 7.8-16.3 gallic acid equivalents and total flavonoid contents, 1.59-4.86 catechin equivalents. Reducing power at 10 mg/ml extract concentration ranged from 1.34 to 1.84. Extraction efficacy of components with antioxidative

properties was lowering in the following order: hexane> chloroform> ethanol> water. *A. Arabica* bark has the highest amounts of total phenolics, ranging from 0.004/g.

In-vitro DPPH free radical scavenging activity of the methanolic extract of all the parts of *Acacia Arabica* were compared with ascorbic acid and quercitin (Standard used) was observed which showed that extract of Arabica leaf shows higher activity followed by bark and twigs. At the concentration of 0.1 mg/ml the scavenging activity of the leaf reached 61.24%, while at the same concentration bark and twig have 52.3% and 52.35% activity.

Keywords: Acacia Arabica, Flavonoid, Catechin, Quercitin.

An overview of Photosensitizers: Their use in photodynamic therapy for communicable and non-communicable diseases

Gupta Megha*, Tripathi Pankaj

Department of biotechnology, Invertis University, Bareilly, U.P., India 243123, meghagupta110@gmail.com, pankaj.t@invertis.org

ABSTRACT

Photosensitizer is the chemical molecule which is light sensitive, also known as photosensitizing agent or drug when used in photodynamic therapy. It can be used as both topical and systemic sensitizing drug. It absorbed light of the particular wavelength and produces significant response against targeted tissue or cell which contains it. Photosensitizer uses the light energy to generate photochemical reaction to produce reactive oxygen species. Activated photosensitizer transfers from its low energy state to high energy state and then an excited triplet state. Molecular oxygen is present at its triplet state when the photosensitizer and an oxygen molecule interacts, an energy change can take place that allows the photosensitizer to relax to its low energy state, and create an excited singlet state oxygen molecule. In photo dynamic activation, a wavelength range of 405-900 nm is generally used for the photosensitizer excitation. Different penetration depth occurs in this range. The significant factors consider for the use of this wavelength range are depth of penetration we need to excite the photosensitizer and the absorption rate of photosensitizer. After the administration of photosensitizer agent in body, it remains longer in target cell comparison to normal cell. A perfect photosensitizer would be activated on specific wavelength of light and shows no cytotoxicity in absence of light which prevents unexpected treatment. Perfect photosensitizer absorbed light at wavelength 650 to 800 nm because absorption of single photons with wavelengths longer than 800 nm does not provide enough energy to excite oxygen to its singlet state. Although it used to be considered desirable for the interval between drug administration and irradiation (drug–light interval, DLI) to be as long as possible (up to 4 days), so that the PS was given sufficient time to clear from normal tissues, while remaining concentrated in tumors.

Keywords-Photosensitizer

Regulation of Glucose By G3pp Enzyme

Neetu, Kiran, Babita, Gurpreet, Avanish, Sachin Srivastava

Department Of Biotechnology, Invertis Institute Of Engineering And Technology(IIET), Invertis village, Bareilly- Lucknow NH24, Bareilly, INDIA.
E-mail: Sachin.s@invertis.org

ABSTRACT

Enzymes are responsible for catalysing reactions in a variety of processes (biological process) in all living cells. Enzymes are catalysts as they can accelerate the rate of reaction. Insulin is used to maintain the sugar level in the body. But when insulin fail to maintain the glucose level, then an enzyme name g3pp (glycerol-3-phosphate phosphatase) maintains the excess glucose level and protect the cells (beta cells) and organs of the body. By converting glucose into glycerol, g3pp prevents excessive formation and storage of fat and also lowers the excessive production of glucose in liver which is a major problem in diabetes. G3PP enzyme has the ability to breakdown the excess glucose and diverts it outside the cells and protects the organs (pancreas, liver) from harmful effects of excess glucose.

The paper reveals that how g3pp enzyme regulate the glucose level. G3pp enzyme able to break down the excess glycerol phosphate to glycerol and divert it outside the cell and thus protecting the insulin-producing beta cells of the pancreas and various organs from the toxic effects of high blood glucose levels. G3pp protects the beta cells and various organs of the body.

G3pp enzyme is a solution for diabetic patients and a remedy for high glucose level in the body. This enzyme able to regulate the glucose level as well as fat and converts the glucose and fat into another compounds in the body. G3pp enzyme prevents excessive formation and storage of fat and also lowers the excess level of glucose. It is concluded that g3pp enzyme can be used to regulate the level of glucose and fat and can be used as a remedy for diabetes. G3pp enzyme protects from the harmful effects of glycerol phosphate and protects the organs and cells of the body. G3pp enzyme can protect the peoples from poisonous effects of glucose and regulate the sugar level.

Keywords: glucose, diabetes.

Up-regulation of fibroblast growth factor receptor 1 due to prenatal tobacco smoke exposure mediates developmental defects in new born

Pallavi Saxena[1], Dibyabhaba Pradhan[2], Rashi Verma[2], Shashi N Kumar[2], Arun Kumar Jain[2], Ravi Deval[1]

[1]Department of Biotechnology, Invertis University, [2]Biomedical Informatics Centre, National Institute of Pathology, ICMR

E-mail: pallavi.saxena0404@gmail.com

ABSTRACT

Tobacco-smoking is the most important risk factor for low birth weight, pre-term delivery, congenital anomalies, pregnancy loss and fetal growth. It was estimated that approximately 30% of growth-restricted neonates could be independently associated with maternal smoking. This study was aimed to examine the prenatal tobacco exposure on mRNA expression in the umbilical cord tissue. Gene Expression Omnibus-GSE 11798 data was retrieved to perform gene expression profiling using Bioconductor package limma. Twenty-six genes were found to be differentially expressed (fold change≥ 1.5 and corrected p value<0.05) in tissues obtained from smokers category. Myosin heavy polypeptide-11(MYH11) that is responsible for haematopoiesis is observed to be highly up-regulated while Carcino-embryonic antigen related CAM6 (CEACAM6) that play significant role in maintaining tissue architecture is substantially down regulated. The dysregulated genes were observed to participate in biological processes / pathways related to growth releasing hormone, angiogenesis and embryonic skeletal and cardiac development. Network analyses of 26 differentially expressed genes were carried out using Cytoscape. Fibroblast Growth Factor Receptor-1 (FGFR1) was identified to be the hub node with 297 interacting partners, which regulates transcription, cell growth, differentiation and apoptosis. The upregulation of FGFR1 in umbilical cord tissue may lead to future health complications such as encephalocraniocutaneous lipomatosis, osteoglophonic dysplasia and Pfeiffer syndrome in new born. The findings open up possibility of overcoming these adverse health effects through FGFR1 targeted therapies during pregnancy.

Keywords: Tobacco exposure, birth weight, pregnancy outcome, umbilical cord

Bacillus Thuringiensis and Its Pesticidal Crystal Proteins: A Review

Ruchi Singh*, Dinesh Kumar, Jaspal Singh

Department of Biotechnology Invertis University Bareilly 243123, Email:lfclub.ruchi@gmail.com

ABSTRACT

Bacillus Thuringiensis,first isolated by Shigetane Ishiwatari (1901). It is a gram positive, facultative aerobic, rod like, motile and sporulating bacterium. *Bt* is a naturally occurring soil borne bacterium that is found worldwide. It produces crystal of endotoxin (Cry protein or delta toxin) toxic to insect mainly in their larval stage, thus they act as insecticide. These crystal proteins (cry protein) are insect stomach poisons. It is an important biological insect control agent, sometimes referred as insecticidal crystal protein (ICP) as protein formed during sporulation in some *Bt* strains coded by cry genes. These crystal proteins are toxic to very specific species of insects yet harmless to humans and the natural enemies of many crop pests. Since 1996 plants have been modified with short sequences of genes from *Bt* to express the crystal protein *Bt* makes. With this method, plants themselves can produce the proteins and protect themselves from insects without any external *Bt* and/or synthetic pesticide sprays. In 1999, 29 million acres of *Bt* corn, potato and cotton were grown globally. It has been estimated that by using *Bt* protected cotton, the United States was able to save approximately $92 million. *Bt* GM crops are protected specifically against European corn borer, southwestern corn borer, tobacco budworm, cotton bollworm, pink bollworm and the Colorado potato beetle. Other benefits attributed to using *Bt* include: Reduced environmental impacts from pesticides – When the plants are producing the toxins in their tissues there is no need to spray synthetic pesticides or apply *Bt* mixtures typically. *Bt* transgenic crops have been overwhelmingly successful and beneficial, leading to higher yields and reducing the use of chemical pesticides and fossil fuels. However, under development has attracted some criticism particularly with regards to the potential evolution of pest-resistant insect strains.

Keywords- *Bacillus Thuringiensis,* Cry protein, transgenic crops

Effect of sugarcane yellow leaf syndrome on sugarcane (*saccharum officinarum linn.)* growth in Uttar Pradesh

Keshav Shukla[1], Sanjeev Kumar Maurya[1] and Keshav Prasad Pandey[2]

[1]Department of Biotechnology, Invertis University, Bareilly, UP, India, [2]UP Council of sugarcane research, Shahjahanpur, UP, India

Corresponding author: keshavshukla1689@gmail.com

ABSTRACT

In India four states including Uttar Pradesh SCYLV was very first reported in 2000. A field experiment has been done to assess the impact of SCYLV on agronomic characteristics of sugarcane. The characteristics of SCYLV-infected plants were compared to those of virus-free plants collected from the various zones of Uttar Pradesh; on various growth parameters of sugarcane viz. juice quality, cane yield and cane quality for varieties CoS 08272, Co 0238, CoS 8436 and CoS 767.

Significant reduction in stalk weight were detected for cultivar CoS 8436 and CoS 767 (28%, and 22% respectively but not for either of the two other cultivars. In the first ratoon crop the reduction in stalk weight were recorded CoS 8436 (32 %), CoS 767 (27 %) and also for CoS 08272 (7.5%) and Co 0238 (6%). There is also significant reduction in amount and quality of cane juice was observed in CoS 8436 (11 %) and CoS 767 (9 %). There is no significant reduction in the observed parameters were observed in CoS 08272 and Co 0238, although reduction in stalk height and diameter were recorded in infected canes of these cultivars in the first ratoon.

Keywords: SCYLV, CoS 08272, Co 0238, CoS 8436 and CoS 767.

Think Before You Take A Breath: Adverse Effects of Air Pollution

Sachin Kumar Srivastav[1], Namrata Kulshreshtha[2*] and Prof. R. C. Vaishya[2]

[1]Department of Biotechnology, Invertis Institute of Humanities and Applied Science, Invertis University, Bareilly- Lucknow National Highway-24 Bareilly (U.P) -243123 India

[2]Department of Civil Engineering, Motilal Nehru National Institute of Technology, Allahabad

Mail ID rce1505@mnnit.ac.in

ABSTRACT

Air pollution is not just a health risk, but also a hindrance to development. By causing illness and premature death, air pollution reduces the quality of life.Air pollution has emerged as a worldwide problem and deterioration of air quality leads to health problems in humans, all living organisms and plants. Recent research works have reported various harmful effects and danger associated with increasing amount of criteria pollutants in the air.Long–term exposure to environmental pollutants was also associated with increased risk of mortality for many types of cancer. Researchers have found significant amounts of potentially toxic magnetic nanoparticles in human brain.These particlesare produced during combustion and can reach high levels in polluted areas. The research has shown that this might have the possibility of developing Alzheimer-like changes in the brain.The increasing concentration of pollutants in the atmosphere, mainly NO_2 and particulate matter, indicates the risk of developing insulin resistance as a pre-diabetic state of type 2 diabetes in adults as well as in children. Scientists also reported that Pregnant women exposed to high levels of air pollution are twice as likely to deliver a kid with autism and low birth weight compared to women exposed to low stages. Researchers also identified a 19% higher risk of women giving birth prematurely if they are exposed to fine particle air pollution during pregnancy.Air pollution has also been identified for the first time as a major contributor tostroke leading to death and disability, mainly in developing and middle-income countries like India. Recently, according to the report of WHO, 2015, 13 of the world's 20 most-polluted cities are in India. The time has now come to consider abatement of "Air Pollution" as a priority and tighter air pollution standards may save thousands of lives, greatly improve public health.

Keywords: Air pollution, Particulate matter,Pregnant women, Deaths, Fine particulate pollution.

Mathematical Modeling of DNA Structure, Dynamics and Mechanics

Musharraf Ali
Department of Mathematics, Gandhi Faiz-e-Aam College, Shajahanpur-242001
(Affiliated to M.J.P. Rohilkhand University, Bareilly, U.P., India)
E-mail: drmusharrafali@gmail.com

ABSTRACT

This paper presents the main concepts, ideas and result in the fields of DNA topology, elasticity mechanics and statistical mechanics. Discussion includes the notions of the linking number and twist of closed DNA, elastic rod models, sequence dependent base-pair level models, statistical models such as helical worm-like chain and freely jointed chain and dynamical simulation procedures. Experimental methods that lead to the development of the models and the implications of the models are also discussed.

Keywords: Elasticity, Mechanics, Statistical mechanics, DNA topology

Signatures of natural selection in the drug metabolizing enzyme genes

Sheikh Nizamuddin, K. Thangaraj
CSIR-Centre for Cellular and Molecular Biology, Hyderabad, Telangana, India
Mail ID: snizam001@gmail.com

ABSTRACT

During the course of migration and colonization, modern human experienced various selective pressures; including range of xenobiotics which contributed to heterogeneity of drug response in contemporary populations. Many genes that have influence on drug response are designated as ADME genes (absorption, digestion, metabolism and excretion of the drug) and are divided into core, extended, phase-I, phase-II and modifiers. Of which, modifiers alters the biochemical function of other genes and have excess of positive natural selection (median stdz-core=0.033±0.95; p-value=1.7×10^{-9}-3.7×10^{-3}). Taxane and statin drugs primarily used for chemotherapy and lowering cholesterol level, respectively; and well known for heterogeneous drug response in world populations. We observed that taxane and statins pharmacokinetic pathways are under natural selection (p-value=$2.53\times10^{-9}$and 2.73×10^{-9}-1.09×10^{-4}; q-value=1.28×10^{-7} and 6.91×10^{-6}-1.1×10^{-3}). Interestingly, both of these drugs are having natural resource. Besides these, we observed signal of selection in Ibuprofen pharmacokinetics (p-value=1.76×10^{-5}; q-value =2.22×10^{-4}), beta-agonist/beta-blocker pharmacodynamic (p-value=4.79×10^{-4}; q-value =4.04×10^{-4}) and Zidovudin pharmacokinetics/dynamic pathway (p-value=7.0×10^{-4}; q-value =5.06×10^{-4}). In selection sweep analysis, we observed hard sweeps signals in a total of 322 loci (std-z score>3). Of which, 53 affect mRNA expression (p-value<0.001) and 16 were already reported with therapeutic response and metabolism of drug/organic molecules. Interestingly, we observed that African population have experience to 2 phases of natural selection, one at ~30 thousand another at ~10 thousand years before present, which imply that left behind populations of Africa survived and experience different selective pressure compared to "out-of-Africans".

Analysis of Glaucoma at Genome level

Mudasir Ahmad Shah, Raja Ishaq Nabi Khan, Waseem Akram Malla and Sheikh Firdous Ahmad
Indian Veterinary Research Institute, Indian Council of Agriculture Research (ICAR), Izatnagar 243 122, Bareilly (UP), India.

ABSTRACT

Genetic and genomic studies, including genome-wide association studies (GWAS) have accelerated the discovery of genes contributing to glaucoma, the leading cause of irreversible blindness world-wide. Glaucoma can occur at all ages, with Mendelian inheritance typical for the rare early onset disease (before age 40) and complex inheritance evident in common adult-onset forms of disease. Recent studies have suggested possible therapeutic targets for some patients with early-onset glaucoma based on the molecular and cellular events caused by

MYOC, OPTN and TBK1 mutations. Diagnostic genetic tests using early-onset glaucoma genes are also proving useful for pre-symptomatic disease detection and genetic counseling. Recent GWAS completed for three types of common adult-onset glaucoma have identified novel loci for POAG (primary-open-angle glaucoma) (ABCA1, AFAP1, GMDS, PMM2, TGFBR3, FNDC3B, ARHGEF12, GAS7, FOXC1, ATXN2, TXNRD2); PACG (primary angle-closure glaucoma (EPDR1, CHAT, GLIS3, FERMT2, DPM2-FAM102); and exfoliation syndrome (XFS) glaucoma (CACNA1A). In total sixteen genomic regions have been associated with POAG (including the normal tension glaucoma (NTG) subgroup), 8 with PACG and 2 with XFS. These studies are defining important biological pathways and processes that contribute to disease pathogenesis.

An Approach of Pattern Mixture Model (PPM) For Sensitivity Analysis In Case of Missing Data

Gaurav Shukla[1], Pankaj Tiwari[2] and Shuchita Gupta[3]

[1]Department of Management, Invertis University, Bareilly

[2]Biostatistician, Cognizant Technology Solutions, Mumbai

[3]Department of Applied Science & Humanities, Invertis University, Bareilly

ABSTRACT

Analysis of missing data is very crucial part of clinical trials. Over the past years regulators, practitioners, and academicians in the pharmaceutical industry has recognized the need of rigorous, transparent, clearly interpretable, and scientifically justified methodology for preventing and dealing with missing data in clinical trials. The new guidelines and recommendations are focusing not only to carefully select the methods that are based on strong statistical assumptions regarding the missingness methods, for analyzing the primary endpoint for the study but also on the requirement basis to perform the sensitivity analysis that stress-test the results of the primary analysis under the different sets of assumptions. There are so many methods that could be used for sensitivity analysis but some of them not yet gained a wide spread -usage due to their underlying complexity theory, and partly because of lack of relatively easy approaches to their implementation. Here, we are presenting the several tactics for handling the missing data on the basis of pattern mixture model (PPM) using procedure of SAS/STAT. Pattern mixture models provide flexible framework for sensitivity analysis that allows formulating assumptions regarding missing data in a transparent and clinically interpretable manner.

Computational Method for surface structure prediction and revealing protein-ligand interaction from bacterial derived DyP Type Peroxidase

Anil Kumar Singh* [1], Abhay Raj [2]

[1 and 2] Environmental Microbiology Laboratory, Environmental Toxicology Group CSIR-Indian Institute of Toxicology Research (CSIR-IITR), Vishvigyan Bhawan, 31, Mahatma Gandhi Marg, Lucknow-226001, Uttar Pradesh, India.

1Academy of Scientific and Innovative Research (AcSIR), CSIR-IITR, Campus Lucknow- 226001, Uttar Pradesh, India.

Presenting author: Anil Kumar Singh*

phd.anil@yahoo.com

ABSTRACT

DyP type peroxidase regard as highly efficient and specific catalyst for catalysis of Lignin, dye and phenolic compounds. Bacteria are currently being focused for their Dyp-type peroxidase enzyme production and exploited for biodegradation of toxic lignin and other phenolic compounds. DyP type peroxidase is a heme containing enzyme having highly catalysis properties for its substrate. Three-dimensional structural analysis for cavity or active site prediction is a highly challenging task to researcher. Three-dimensional structure of DyP type peroxidase, responsible for its specific biological feature. specific constituent ingredients of amino acids contribute to form binding cavity

within this molecule. active site prediction provides the constitutional information of amino acids residue which participates in binding and catalysis process that's governs by this protein molecule. Recognition of functional information for a DyP- Peroxidase from its three-dimensional (3D) structure is also a challenging task. (http://projects.biotec.tu-dresden.de/metapocket/) metaPocket server computes the cavities in a given protein modeled pdb. Once the pdb file input and submit server computes protein atoms and recognize the functional sites in DyP type Peroxidase protein molecule. Processed pdb model file subjected to visualization with molecular graphics visualization tools. Ligand interaction with cavity forming amino acid residues visualized within surface structure. Different biochemical properties highlighted for ligand interaction, distance, and polar contracts. Exploration of functional site in surface structure form provides cavity visualization and ligand interaction in protein molecules. Structural information revealed cavity forming amino acids and ligand interaction which initiate the biochemical catalysis of DyP type Peroxidase enzyme with its substrate.

Keywords: DyP type Peroxidase, PyMOL, Binding pockets, metaPocket server,UCSF ChimeraX.

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Osmolytes in Cell Volume Regulation

Nitesh Kumar Poddar*, Yasanandana Supunsiri Wijayasinghe$^{\Psi}$ and Arti Tyagi*

*Department of Biotechnology, Invertis University, Bareilly, Uttar Pradesh-243123, India

ψDepartment of Biochemistry and Clinical Chemistry, Faculty of Medicine, University of Kelaniya, Ragama, Sri Lanka

E-mail: nitesh.p@invertis.org, niteshpoddar@gmail.com

ABSTRACT

Osmolytes are small molecules or ions dissolved in cellular or extracellular fluid of all forms of living things to maintain the cellular volume. Other than volume regulation, osmolytes has variety of roles in biological systems including protein folding, protein disaggregation, protein-protein interaction, and protection against high osmotic environments. Nature has selected organic osmolytes for these functions over the inorganic ions due to several reasons. Naturally occurring osmolytes belong to four chemical classes namely polyols, sugars, amino acids, and methylamines. Osmolytes like trehalose, glycine betaine and proline, help protect organisms from stresses. In certain instances, osmolytes are used to determine the maximum depth up to which a fish can survive in the marine eco-system. Methylamines like trimethylamine N-oxide, glycerophosphocholine (GPC) are counteracting the effect of high urea concentrations in renal cells of animals. Some organisms use higher amounts of osmolytes and different varieties of osmolytes than others as an adaptation to the environment where organism resides. In this chapter up to date knowledge of biological roles of diverse organic osmolytes are being discussed in details.

Keywords: osmoregulation, osmolytes, proline, trehalose, glycine betaine, taurine, salt, osmolarity, transporter

Small anti-oxidant chaperones in TTR amyloidosis: an approach toward therapeutic intervention of senile systemic amyloidosis

Sheeza Khan$^{\delta}$, Dr. Nitesh Poddar* and Laishram Rajenderkumar Singh$^{\delta}$

$^{\delta}$Dr. B. R. Ambedkar Center for Biomedical Research, University of Delhi, Delhi-110007

*Department of Biotechnology, Invertis University, Bareilly, Uttar Pradesh-243123

lairksingh@gmail.com

ABSTRACT

Senile Systemic Amyloidosis (SSA), frequently diagnosed as a restrictive cardiomyopathy, is most commonly reported in men over the age of 60 years and symptoms include congestive heart failure, arrhythmias, and conduction defects. It is caused due to the deposition of wild type transthyretin (TTR) amyloids in the heart. In SSA, the heart is the predominant site of deposition of the TTR amyloid which disrupts the normal cellular processes and tissue functioning of this organ. TTR is a 55 kDa homotetrameric protein responsible for the transport of

thyroid hormones and retinol binding protein. TTR is present in serum and cerebrospinal fluid synthesized by liver and choroid plexus in brain. Much effort has been made towards identifying strategies for preventing TTR aggregation. Some small molecule drugs have already been discovered to have the potential to inhibit TTR aggregation. These includes NSAIDS, polyphenols, some herbal drugs etc. However, their use for the therapeutic interventions has been challenged due to high toxicity, low efficacy and practicability to reach target organ. Since, oxidative stress is one of the important causes of amyloid-induced toxicity, it is important to look for drugs that have anti-oxidant property and also are capable of suppressing or inhibiting aggregation of proteins. In the light of this, in the present proposal we plan to investigate the effect of naturally occurring small anti-oxidant chaperones on the aggregation behavior of TTR.

Methodology:

Heat-induced denaturation studies, CD and Fluorescence measurements, Time-dependent aggregation kinetics, Dynamic light scattering measurements, ANS binding assay, Thioflavin-T (ThT) assay, Transmission electron microscopy, Oxidative stress marker assay.

Significance of the study:

The study will give a strategy to prevent TTR aggregation. The study will also shed light into the aggregation mechanism in the presence and absence of additives. The study will shed insights for the therapeutic intervention of SSA.

In-vitro analysis of bioactive compounds of *Chlorophytum borivilianum*

Pallavi Sharma[1], Abhinay Kr Singh[2], Dr. SK Maurya[1], Dr. V Singh[2], Dr. NK Poddar[1]

[1]Department of Biotechnology, Invertis University, Bareilly, U.P. (India)

[2]Molecular Research & Development, MRD LifeSciences Pvt Ltd, Lucknow, U.P. (India)

[2]Department of Biotechnology, Institute of Engineering and Technology Lucknow, U.P.

ABSTRACT

Chlorophytum borivilianum, is the one of the wild plant which belongs to the Asparagaceae family. It is very important species and contains exceptional medicinal properties such as antibacterial, antifungal, antiviral, etc. It is used for aphrodisiac, adaptogen, anti-ageing, health restorative and health promoting purposes. The leaf of the C. borivilianum contains alkaloids, glycosides, steroidal nucleus, saponins and tannins. The saponins and alkaloids impart highly medicinal value.

Methodology-The leaf extract was prepared by solvent extraction method by using polar and nonpolar solvents that are, hexane, petroleum ether, ethyl acetate and acetone, and then check their antimicrobial activity against pathogens E. coli, S. aureus, P. aeruginosa employing agar well diffusion method.

Results-With help of thin layer chromatography identify the number of molecules that present in our extracts. Phytochemicals are extracted after 24 hrs they show activity only against E. coli and their zone of inhibition of extracts are 18.5 mm of Hexane extract, 19.5 mm of petroleum ether, 13 mm of ethyl acetate and 17.5 mm of Acetone. Extracts which retrieve after 48 hrs are show the inhibition against all pathogenic bacteria which were taken in our study. Maximum zone of inhibition shown against S. aureus that a range of 20 mm to 24 mm. Detection for the number of molecules of phytochemical is done thin layer chromatography in which it was found that 4 components were present in acetone extract, 2 components in extract of ethyl extract and one components extract of Hexane and Petroleum ether.

Conclusion-From this study found that polar solvents are best for the extracts of phytochemicals and they were shown the best antimicrobial activity as compare to other extracts.

Keywords: - Phytochemicals, Polarity, E. coli, S. aureus, and P. aeruginosa

Analysis of interleukin-23 and 7G10 interactions for computational design of lead antibodies against immune-mediated inflammatory diseases

Noor Saba Khan[1,4] Dibyabhaba Pradhan[1], Rajabrata Bhuyan[2], Tanmaya Kumar Sahu[3], Ravi Deval[4], Nitesh Poddar[4], Arun Kumar Jain[1]

[1]Biomedical Informatics Centre, National Institute of Pathology-ICMR, New Delhi-110029, India
[2]Bioinformatics Infrastructure Facility, University of Kalyani, Kalyani, West Bengal-741235, India
[3]Centre for Agricultural Bioinformatics, ICAR-Indian Agricultural Statistics Research Institute, New Delhi-110012, India
[4]Invertis Village, Bareilly-Lucknow National Highway, NH-24, Bareilly, Uttar Pradesh 243123

ABSTRACT

The wealth of structural data on theurapeutic targets in complex with monoclonal antibodies (mAbs) and advances in molecular modelling algorithms present exciting opptunities in the field of novel biologic design. IL23 is an established drug target of autoimmune diseases. Therefore, IL23 and its mAb, 7G10 complex offers prospect to design potent lead antibodies by exploring the complete epitope-paratope interface. Herein, key interactions aiding antibody based neutralization in IL23-7G10 complex are determined through PyMOL, LigPlot+, Antibody i-Patch, DiscoTope and FoldX. Six amino acids Ser31, Val33, Asn55, Lys59 in heavy chain and His34, Ser93 in light chain are subjected to in silico mutagenesis with residues Met, Trp, Ile, Leu and Arg. A set of 431 mutant macromolecules are designed. Binding affinities of these molecules with IL23 are estimated through protein–protein docking by implementing ZDOCK, ClusPro and RosettaDock. Subsequently, the designed macromolecules showed better binding affinity compared to 7G10 in three docking software are cross validated using binding free-energy calculations by applying Molecular Mechanics/Poisson Boltzman Surface Area method in CHARMM. Thirty nine designed theoretical antibodies showed better binding affinity in all evaluations compared to 7G10. Analysis of ten top ranked molecules and 7G10 showed key residues necessary for IL23 neutralization. Therefore, we propose these molecules have the potential to act as lead antibodies to neutralize IL23.

Keywords: Interleukin23, 7G10, Computer aided antibody design, Antigen-antibody docking, Interaction energy, Binding free energy

High Concentration of Cadmium and Lead affects the development of Placenta of Mothers delivered Low Birth Weight Fetus

Zeba Mueed, AK Jain*, Shashi N Kumar*, Banajit Basita*, Ravi Deval

Department of Biotechnology, Invertis University, Bareilly -243 123
*National Institute of Pathology (ICMR), Safdarjang Hospital Campus,New Delhi 110 029

ABSTRACT

Objective: Quantification of cadmium & lead in maternal blood serum and placentas of mothers delivering neonates with complication of low birth weight (LBW), and to establish association of these toxic elements with placental development.

Methodology: Maternal blood and placenta of 100 mothers delivering neonates with LBW complication and appropriate gestational age deliveries were collected. Cadmium and lead in digested samples were measured by ICP-MS and changes in placenta were analyzed by TEM.

Results: The mean age and mean age at marriage and BMI was significantly less (P<0.001) in case of LBW group as compared to AGA group. It was also observed that the mean of birth weight, body length and head circumference was significantly less in LBW foetus as compared to AGA foetus. Placental parameters like placental weight, diameter, thickness, number of cotyledons and cord length & diameter was also significantly less in LBW. As per the route of blood flow during pregnancy the concentration of cadmium and lead in maternal serum and placenta in LBW was 8.997ppb & 0.236ppm and 38.210ppb & 0.675ppm respectively while in case of AGA it was 3.602ppb & 0.109ppm and 23.351ppb & 0.426ppm respectively, which was significantly high in all LBW samples as compared to samples collected from the patients having AGA delivery. Altered ultrastructural characteristics were also observed in the tertiary villi of LBW group placenta which included irregularly distributed, blunt tipped & sometimes broken villi, more incidence of syncytial knots, less number of cell organelles, occurrence of hyperplasia of cytotrophoblastic cells, zigzac nature basement membrane, endothelial cells protrusion into the lumen, more number of VSM, more incidence of degenerated nuclei, etc. Presence of these characteristic features in LBW placenta, ultimately results in limited nutrient transfer and reduced blood flow to the foetus.

Conclusion: After excluding all the known factors of LBW, except genetic, observations and data from this study shows that significantly high concentration of Cd & Pb influence placental angiogenesis, evident by the ultrastructural abnormalities in LBW placenta, may be the major factor attributed towards the occurrence of LBW deliveries.

Keywords: LBW, AGA, Placenta, Cd, Pd.

Maturity stages influencing the ascorbic acid content in Guava cultivars

Surabhi Shukla, Devinder Kaur
Centre of Food Technology, University of Allahabad, INDIA.
E-mail: surabhishukla22@gmail.com

ABSTRACT

Introduction-Guava (Psidium guajava) is an important tropical fruit of family Myrtaceae. Guavas are considered excellent sources of antioxidant phytochemicals, which include ascorbic acid, carotenoids, antioxidant dietary fiber, and polyphenolics. high concentration of polyphenolic antioxidants for example ascorbic acid, flavonoids and phenolic acids in guava and Indian gooseberry make these fruits attractive for consumers. Changes in ascorbic acid content of five Guava cultivars (Lalit, Allahabad Surkha, Red fleshed, Chittidar and Safeda) were studied at three different ripening stages (unripe, semi-ripe and ripe).

Material and method- Ascorbic acid was estimated by 2, 6 dichlorophenol indophenol titration method. Sample (10 g) was prepared in 3% (w/v) metaphosphoric acid and the volume was made upto 100 ml with metaphosphoric acid. Filtered aliquot (5 ml) of sample was titrated against standard 2, 6 dichlorophenol indophenol (2, 6 DCIP) dye solution until the pink color developed completely. **Result and discussion**- The results obtained from the ascorbic acid assay demonstrated that the ripe stage had higher value of ascorbic acid content in white fleshed cultivar Safeda and Lalit as compare to the red fleshed cultivars Surkha, Chittidar and Red fleshed. The unripe and semi-ripe stages of maturity reported less ascorbic acid content.

Keywords: Guava, ascorbic acid, polyphenols, maturity stages, cultivars

Integration and success of metagenomics and the proteome for recognizing functional microbiome

Sonika Maheshwari, Honey Varshney, Kapil Dev, Mehvi Zaidi, Vishva Pratap Singh, *Sagar Chhabra
Department Of Biotechnology, Invertis University, Bareilly (U.P) India.
*E-mail: sagar.c@invertis.org

ABSTRACT

Introduction: There is immense diversity of uncultivable microorganisms present in environment and isolated from sources such as plant, animal and as human microbiome. The development of high-throughput taxonomic DNA sequencing methods generate a large amount of data however are limited on functional assignments to identify role of these microorganisms. In this study we applied tools for assignment of function to rhizosphere microbial metagenome DNA cloned in a Fosmid based vector and expressed in bacterial host *Escherichia coli*. The recombinant DNA clones were selected using functional assays such as mineral phosphate solubilization (MPS) trait are also being tested for antibiotic resistance, secondary metabolite production. The selected assignment of functional genes of 7 metagenome clones and the success to integrate proteomics to this approach will be presented during the conference. **Materials and Methods**: The gene calling of sequenced data was carried out using the Fgenesb annotator pipeline. Homology searches for deduced proteins were performed by searching against the nonredundant database sourced from the nucleotide (nr/nt) collection using the BLAST program. The annotation of contigs was carried out using an online trial version of CLC workbench.Results: 7 out of 18,000 selected clones sequenced recognized MPS and other gene targets from the rhizosphere metagenome. **Conclusion**: Integrating proteome analysis on functional metagenome can be a useful approach to study microbial functions.

Keywords: Metagenomics, Functional assay, Metagenome

Protein Deficiency in Juveniles

Neel Mani Tripathi
Department of Law, University of Allahabad, INDIA.
E-mail: advnmani@gmail.com

ABSTRACT

There is an interactive mechanism by which diet and nutrition can lead to behavioural outcomes in juveniles such as aggression, delinquency, hyperactivity, and anti-social behaviour which lead to criminal behaviour in later life. Dopamine and serotonin are the two major monoamine neurotransmitters that are known to be mood stabilizer. The dysfunctional interactions between serotonin and dopamine systems in the prefrontal cortex may be an important mechanism underlying the link between impulsive aggression and its comorbid disorders. Specifically, serotonin hypofunction may represent a biochemical trait that predisposes individuals to impulsive aggression, with dopamine hyperfunction contributing in an additive fashion to the serotonergic deficit. It has been suggested that protein foods which are made from the building blocks of amino acids (including tyrosine and tryptophan) may boost dopamine and serotonin production without increasing appetite. Therefore it has been suggested to take a high protein breakfast including eggs, lean meats and dairy was best at reducing mid-morning cravings whilst increasing dopamine levels. Serotonin isn't found in foods, but tryptophan is, therefore serotonin levels can be increased by eating meals rich in tryptophan i.e., cheese, pineapple, tofu, turkey, salmon. Other ways to boost the levels of neurotransmittors comprises of exercise, sunshine (light therapy) and supplement diet with probiotics which in turn manages the gut-brain axis.

Keywords: Dopamine, Serotonin, Juvenile.

Therapeutic Approach of Osmolytes in Treating Immunological Disorders

ZebaMueed, Ayushi Saxena, Ravi Deval, Nitesh Poddar
Department of Biotechnology, Invertis University, Bareilly - 243 123, INDIA.
E-mail: nitesh.p@invertis.org

ABSTRACT

Pathogenic microbes are constantly evolving and so as to cope up with this our immune system has also evolved to protect the host organism with the help of osmolytes. Osmolytes are naturally organic compound of different chemical classes such as amino acids, methylamines and polyols. High concentrations of osmolytes can cause structural changes in cellular proteins. In recent studies it has been seen that osmolytes are involved in protein folding, protein disaggregation and protein-protein interaction, for example Ag-Ab interaction, inflammatory response. Many diseases are caused due to formation and degradation of aggregates in related proteins. Since osmolytes play an important role in regulating immune system, they can be used in drug development and drug targets.For protection of host from variety of diseases and normal immunocompetence, adequate dietary provision of all amino acids is required. **Scope:** The levels of detoxification of free radicals and reactive oxygen species are maintained by cysteine which is also a rate-limiting component of glutathione synthesis. The difference between macrophages and cysteine transport activities of T cell enables T cell to switch between prooxidant and antioxidants. Studies have shown that cysteine supply is impaired with HIV thus N-acetyl cysteine (NAC) is a drug that can be considered for treatment of HIV infection. Researches on osmolytes and their role in regulation of immune system have shown that IgA production is increased in sera and intestinal tissues by diet supplementation with beatine. **Conclusion:** Hence researches on osmolytes are beneficial for developing drugs to treat various immunological disorders.

Keywords: Osmolyte, Immune system, Cysteine.