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Genomics India 2023

Welcome to GIC 2023

The two-day genomics conference aims to bring together industry, academia and research that will feature informative talks on current trends and advancements in genomics. The gathering of renowned speakers will explore the latest research into indigenous products that address local needs. The conference will feature cutting-edge research into the latest advances in genomic technologies, with a focus on sharing path-breaking findings.

The conference will feature panel discussions and parallel discussions on 3rd Generation Sequencing, Modern Genomics, Genomics for Agriculture, Diagnostics, Startups, Biotech education and more by Key Opinion Leaders from the industry and academia. The conference will provide an unlimited opportunity to interact with experts from across the industry, including academic, startups and profit and non-profit organisations of the Biotech sector.

We welcome Faculty, students, Post-Doc's, healthcare professionals, industrial R&D professionals, Biotech start-up's and Entrepreneurs.

NEARLY THREE DECADES OF GENOMICS - LOOKING BACK & MOVING FORWARD

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TALK TITLES

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Glimpses into the methylome of Plasmodium from Clinical isolates
Prof Ashis Kumar Das, Birla Institute of Technology & Science, Pilani, India

SARS-CoV2 infection induces microbial dysbiosis in patients with COVID-19
Dr Punit Prasad, Institute of LifeSciences, Bhuwaneshwar, India

Epigenetics: Manipulating genes through physical activity and exercise
Dr Michael Sagner, Director of the European Society of Preventive Medicine

Role of Genomics in Forest Tree Breeding
Dr Yasodha Ramaswamy, IFGTB, Coimbatore, INDIA

Design and Development of Novel Recombinant Protein sub-unit vaccines
Dr Chakshumathi Ghadiyaram, Mynvax Private Limited, Bengaluru, India

Genomics accelerated seed product development
Dr Satish Kanuganti, Rallis India

Genomics in India- a vanguard of modern healthcare: a tale of two diseases
Dr Harsh Sheth, FRIGE House- IHG

Adipocyte-derived Exosomes in Obesity: The Talk between Tissues and Generations
Dr Robert Freishtat, Children's National Hospital,USA

Determinants of Prakriti – a roadmap to personalized medicine
Prof Kapaettu Satyamoorthy, MAHE Manipal

Neurogenomics: Unraveling genic links to neurodegeneration
Dr Mohammed Faruq, CSIR-IGIB

On the Genome and Transcriptome of Mycobacterium leprae; towards understanding genetic mechanisms of reactions and drug resistance in leprosy.
Dr Madhusmita Das, SIHRLC

Capacity-building in genomic surveillance of infectious diseases in Peru.
Dr Stella Chenet, URP, Peru

cardiomyopathies – is there something beyond clinico-pathological features?
Dr Pradeep Vaideeswar, Seth GS Medical College

Genetic diagnosis in brain disorders
Dr Meera Purushottam, NIMHANS

Towards understanding the auditory genetic code
Prof Anuranjan Anand, JNCASR

Vaccine Development and Innovation – pre & post COVID-19 pandemic
Dr Umesh Shaligram, Serum Institute of India, Pune, India

Genome dynamics of enteric pathogens with special reference to antimicrobial resistance
Prof Niyaz Ahmed, University of Hyderabad

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NEARLY THREE DECADES OF GENOMICS - LOOKING BACK & MOVING FORWARD

ENABLING PRECISION MEDICINE FOR ORAL CANCER
Prof Partha Majumder, NIBMG

Data Driven Genomic Application in Clinical Practice" - A multidisciplinary approach
Dr BS Ajaikumar, HCG

Data governance at the intersection of genomic and digital revolutions
Dr Anurag Agarwal, Ashoka University

Bringing scale efficiencies to Omics
Dr Manoj Gopalkrishnan, Algorithmic Biologics

Insights into circulating SARS-CoV-2 variants, immune escape from mAb therapy and the dynamics of coinfection with H1N1-InfluenzaA
Dr Krishna Khairnar, CSIR-NEERI

Genomics, Surveillance and Epidemiology of Emerging Infectious Diseases
Dr Vinod Scaria, CSIR-IGIB

Integrated genomic surveillance - an era to leverage molecular technology to track existing pandemics and predict future ones
Dr Praveen KS, PATH South Asia

Dissecting stem cell heterogeneity and their metabolic states in planaria using single cell transcriptome approaches
Dr Dasaradhi Palakodeti, INSTEM

Correlation of the unique phenotypes of an aggressive plant pest, the mealybug, with its genomic features.
Prof Vani Brahmachari, University of Delhi

Human immune monitoring to emergent vaccines and disease at the cellular and molecular level: lessons from. COVID19 AND TB
Dr Annapurna Vyakarnam, King's College, London

Molecular surveillance of antimalarial resistance from Indian P. falciparum isolates
Dr Praveen K Bharti, ICMR-NIMR

Gene therapy for an inherited eye disorder and mitochondriopathy
Dr P. Sundaresan, AMRF

Advanced computational approaches for chromosome-scale haplotype-resolved genomics
Dr Shilpa Garg, DTU, Denmark

GeneCards expands to genomic "dark matter": Enhancers and ncRNAs
Prof Doron Lancet,Weizmann Institute of Science, Israel

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NEARLY THREE DECADES OF GENOMICS - LOOKING BACK & MOVING FORWARD

Employing high throughput and single cell genomics in studying early vertebrate embryogenesis Prof Sanjeev Galande, Shiv Nadar University
Precision Medicine in understudied/founder populations Dr Kashyap Krishnasamy, Avesthagen Limited
First draft Genome of Punica granatum L. 'Bhagwa' Dr Sushil Middha, MLAC
Nutritional security, Bio-security, Biodiversity perspectives in Sustainable development of Agriculture in India Dr M.S Rao, IIHR, Bengaluru
Analysis of genetic diversity and identification of genome-wide markers associated with foliar disease resistance in Para rubber (Hevea brasiliensis) Dr Bindu Roy, Rubber Research Institute
Rare Genetic Diseases: Challenges Accomplished and the Unmet Needs Dr T L Srinath, GenoPhe Biotech

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Learn from Pacific Bioscience experts about the new paradigms of long read sequencing and data analysis Dr Zuwei Qian, Pacific BioSciences
Long Read Sequencing for whole genome assembly and scaffolding Dr Khi Pin Chua, Pacific BioSciences
Overcoming common challenges and bottlenecks in NGS Library Prep with NEBNext Dr Anuj Gupta, New England Biolabs
DNBSEQ-G99ARS: A novel ultra-fast platform with built-in Bioinformatics module for ultra-fast identification of pathogens using metagenome sequencing data. Dr Ravi Chilukoti, MGI
Agilent Genomics Portfolio: Advancing on a SurePath Dr Rahul Solanki, Agilent
Next-Generation Sequencing (NGS) Basics Dr Raja Mugasimangalam, Genotypic Technology
16S rRNA shotgun sequencing data analysis and Visualization Whole Genome Metagenome - Assembly, Gene prediction and Visualization, Commander Demonstration Dr Prasanna Koti, Genotypic Technology
Insights into Transcriptome and Small RNA data analysis Ms Garima Sanoria, Genotypic Technology
Insights into Whole Genome Sequencing: Alignment to Variant Calling and Reporting Mr Nihar Bachan Das, Genotypic Technology

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SPEAKER ABSTRACTS

NEARLY THREE DECADES OF GENOMICS - LOOKING BACK & MOVING FORWARD

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GeneCards expands to genomic "dark matter": Enhancers and ncRNAs

Doron Lancet, Shalini Aggarwal, Chana Rosenblum, Tsippi Iny-Stein, Marilyn Safran, Ruth Barshir, Shmuel Pietrokovski and Simon Fishilevich
Department of Molecular Genetics, The Weizmann Institute of Science, Rehovot 7610010, Israel

Abstract

The GeneCards Suite (https://www.genecards.org/) is a leading biomedical knowledgebase, with comprehensive and integrated information about human genes (GeneCards, PMID:27322403) and diseases (MalaCards, PMID:27899610). GeneCards is widely used worldwide, with more than 5,000,000 yearly users and >5,000 citations.

Interpreting whole genome sequences (WGS) for disease decipherment is a major challenge: merely ~2% of variants reside in protein-coding territories. To optimize for effective interpretation of functional entities in the remaining “dark matter”, we developed two novel compendia: GeneHancer, for regulatory elements (enhancers and promoters) (PMID:28605766), and GeneCaRNA, for non-coding RNA (ncRNA) genes, respectively occupying 18% and 5% of the genome. GeneCaRNA is unique in being gene-centric, as it directly maps transcript-type genes to mutations defined by DNA coordinates.

GeneHancer is intensively used (>700 citations) for interpretation and discovery of non-coding functional regions in various scenarios. Examples are discovery of recurring structural variants in prostate cancer (PMID:30033370), and identification of an ALS risk gene (*CAV1*) using rare variant burden analysis (PMID:33264630). Novel approaches for decipherment of non-coding variants in rare genetic diseases are critical, as shown in an exome-unsolved study of Primary Familial Brain Calcification (PMID:32506582). With the help of GeneHancer, a deletion of an enhancer of *SLC20A2*, a known protein-coding disease gene, was discovered, showing the same phenotype as *SLC20A2* mutations.

GeneHancer and GeneCaRNA augment by more than an order of magnitude the genomic territories available for disease decipherment via our phenotype interpreter VarElect (PMID:27357693). We have recently augmented VarElect to assume non-coding genes and regulatory elements interpretation capacities. VarElect facilitate fathoming the clinical significance of non-coding variants identified by WGS, often elucidating previously unsolved clinical cases.

Epigenetics: Manipulating genes through physical activity and exercise

Dr Michael Sagner, European Society of Preventive Medicine

Abstract

Many different types of exercise and physical activity induce mechanical, hormonal, and metabolic stimuli that lead to adaptions in almost every tissue and cell type. Recent research has shown that both acute exercise and chronic exercise are potential epigenetic modifiers (affecting DNA methylation, posttranslational histone modifications, and the expression of microRNAs) that change the functional genome in gametes, muscle, blood, and fat cells in brain tissue as well as in cells of the cardiovascular system. Exercise-induced epigenetic modifications may help to treat and prevent pathophysiological alterations of the epigenome in diseases (e.g., cancer, neurodegenerative disorders, cardiovascular diseases).

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Employing high throughput and single cell genomics in studying early vertebrate embryogenesis

Sanjeev Galande1,2
1. Laboratory of Chromatin Biology and Epigenetics, Department of Biology, Indian Institute of Science Education and Research, Pune, 411008, India.
2. Centre of Excellence in Epigenetics, Department of Life Sciences, Shiv Nadar University, Gautam Buddha Nagar, Uttar Pradesh, India.

Abstract

Zygotic genome activation (ZGA) initiates regionalized transcription underlying distinct cellular identities. ZGA is dependent upon dynamic chromatin architecture sculpted by conserved DNA-binding proteins. However, the direct mechanistic link between the onset of ZGA and the tissue-specific transcription remains unclear. Here, we have addressed the involvement of chromatin organizer Satb2 in orchestrating both processes during zebrafish embryogenesis. Integrative analysis of transcriptome, genome-wide occupancy and chromatin accessibility reveals contrasting molecular activities of maternally deposited and zygotically synthesized Satb2. Maternal Satb2 prevents premature transcription of zygotic genes by influencing the interplay between the pluripotency factors. By contrast, zygotic Satb2 activates transcription of the same group of genes during neural crest development and organogenesis. Thus, our comparative analysis of maternal versus zygotic function of Satb2 underscores how these antithetical activities are temporally coordinated and functionally implemented highlighting the evolutionary implications of the biphasic and bimodal regulation of landmark developmental transitions by a single determinant.

Adipocyte-derived Exosomes in Obesity: The Talk between Tissues and Generations

Dr Rob Freishtat
Children's National Hospital Interim Director, Center for Genetic Medicine Research, Washington DC, USA

Abstract

The world is facing a rapidly escalating epidemic of non-communicable diseases (NCDs), including obesity, diabetes, cardiovascular disease, cancer, and neuropsychiatric illnesses. The burden of NCDs is astronomical and treatment is cost-prohibitive for even wealthy countries. This epidemic is associated with rapid socioeconomic and nutritional transitions experienced in both developed and low- and middle-income countries (LMIC) over the last 50 to 70 years. As this epidemic has developed over a minimum of two or three generations, intergenerational and early life (i.e., fetal and childhood) influences are strongly suspected to underlie its cause. These early life influences underlie the Developmental Origins of Health and Disease (DOHaD) conceptual framework that describes how early life environments can impact the development of NCDs throughout the lifespan.

Genomics India 2023

Data-Driven Genomic Application in Clinical Practice – A Multidisciplinary Approach

Dr. B. S. Ajaikumar
HCG, Bengaluru, India

Abstract

The success of “Genomic Medicine” can already be seen in clinical practice and the generalized treatment has shifted towards “genome-immune-based personalized treatment”. An unmet need to efficiently support the work of medical teams is to implement knowledge and data-based molecular tumor boards (MTB) and multidisciplinary clinics (MDT). This multidisciplinary approach of the unified and scientific clinical decision made through harnessing different technological platforms like genomic analysis of tumor tissue and circulating tumor DNA, automating the interpretation and reporting of digital pathology and sequencing data is very important for individualized decision-making, stratifying the patients, and bucketing the cancer treatment.

I will be discussing how such validated, precise, and advanced diagnostics can be used to assess cancer risk, inform prognosis, guide therapy selection and detect disease recurrence after treatment completion. The seamless communication among clinical investigators, pathologists, geneticists through MTB and MDT, and EMR is essential to leverage the collective expertise and link tumor molecular profiles with clinical actions.

Bringing scale efficiencies to Omics

Dr Manoj Gopalkrishnan
CEO at Algorithmic Biologics, India

Abstract

Omics technologies hold great promise for health and wellness. Their cost remains a barrier to more widespread adoption. Algorithmic Biologics is transforming molecular information access through data science. Our patented technology provides scale efficiencies by applying algorithmic ideas like coding-decoding on molecular information while seamlessly integrating with existing workflows and infrastructure. Their SaaS delivered solution is already tested on various platforms, and is CE approved. They are working with 4 out of 5 top genomics companies in the country.

Towards understanding the auditory genetic code

Prof Anuranjan Anand
Jawaharlal Nehru Centre for Advanced Scientific Research (JNCASR) ,Bangalore 560 064 | E-mail: anand@jncasr.ac.in

Abstract

Hereditary hearing loss affects about 1 in 2500 newborns. About 75% of hereditary hearing loss is non-syndromic (NSHL), wherein hearing impairment is not accompanied by any additional clinical phenotype. Genetic causes of NSHL are heterogeneous. Over 125 genes associated with non-syndromic hearing loss (NSHL) have been discovered, to date. To gain an estimate of the contribution of certain genes underlying NSHL, we studied over 500 families with NSHL for pathogenic mutations at the connexin 26 gene- the commonest known cause of NSHL among our populations. Families excluded for connexin 26 gene mutations were examined for a set of additional genes and pursued further for new gene identification where possible. Mutations detected in this relatively small-scale study substantially extend the allelic heterogeneity at the known NSHL genes and provide additional variants for structure-function correlation studies. These findings also have implications for early DNA-based detection of the disorder and genetic counseling of the affected families for implementing suitable intervention strategies.

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Correlation of the unique phenotypes of an aggressive plant pest, the mealybug, with its genomic features.

Vani Brahmachari, Ankita Narang, Surbhi Kohli, Parul Gulati and Jayant Maini*
Dr. B.R. Ambedkar Centre for Biomedical Research, University of Delhi

Abstract

Mealybugs are aggressive pests with world-wide distribution. Our interest in the mealybugs stems from the interesting biology of these insects; genomic imprinting, paternal genome elimination, whole chromosome inactivation and radiation resistance. Paternal genome inactivation in male mealybugs is yet another example of whole chromosome inactivation that is seen in female mammals in the form of X chromosome inactivation. While elegant cytological experiments have implicated histone modification in chromosome inactivation, the molecular basis of the whole chromosome inactivation is yet to be deciphered. It is anticipated that the generation of the resource such as genomic and transcriptome sequence will greatly facilitate these studies in absence of robust genetic approach in this system. We sequenced the genome and the transcriptome; de novo assembled and annotated the genome and analysed the transcriptome of male and female Maconellicoccus hirsutus. Through comparative analysis with four mealybug and eight other insect species, we identified expanded, specific, and contracted gene classes that relate to resistance to pesticides and desiccation. We identified horizontally transferred genes adding to the mutualism between the mealybug and its endosymbionts. The transcriptome analysis indicates the differential expression of genes for sexual dimorphism and also the metabolic pathway genes correlating well with their physiology. The significantly lower expression of endosymbiont genes in males correlates with the depletion of endosymbionts during male development. The presence of a repertoire of non-coding RNA and the homologues of the proteins implicated in X-inactivation as well as DNA methylation status will be discussed in the context of whole chromosome inactivation.

*Current address: Dept. of Biotechnology, Manav Rachna International Institute of Research and Studies, Faridabad.

Genetic diagnosis in brain disorders

Dr Meera Purushottam
Department of Psychiatry, NIMHANS, Bengaluru, India

Abstract

There are brain disorders. There are mental disorders. There are genes in the human genome. Can we match the genes with the disorders? Is there a gene for every condition? Can the same gene cause different conditions? Of both the mind and the brain.

Genomics India 2023

Capacity-building in genomic surveillance of infectious diseases in Peru

Dr Stella Chenet
Instituto de Investigaciones en Ciencias Biomédicas, Universidad Ricardo Palma, Lima, Peru

Abstract

Developing and strengthening the skills, abilities, processes and resources for the genomic surveillance and epidemiological studies of infectious diseases in low and low-middle income countries is a challenging process. The threat of pathogen outbreaks is high and alarming, especially in rural areas of Peru; therefore, implementing the necessary resources for studying these pathogens and getting comprehensive knowledge of their current diversity, drug resistance profile and migratory patterns, allow us to improve the implemented control strategies. Additionally, one of the most important resources that we are still lacking in Peru is the ability to process, comprehend and present genomic data to be applicable for public health decision-making policies. Here, we will tell you about a journey of a group of Peruvian scientist trying to accomplish this process in a hard-to-reach area working hand-to-hand with the regional health authorities and generating collaborative networks for the successful application of genomic platforms for the study of infectious (SARS-CoV-2 and malaria) and neglected tropical diseases (Leishmania, Fasciolasis, Chagas, Dengue and Bartonella). Moreover, one of the major goals of our group proposal is the generation of a bioinformatics hub that could provide assistance to public health authorities in different regions of Peru.

DNBSEQ-G99ARS: A novel ultra-fast platform with built-in Bioinformatics module for ultra-fast identification of pathogens using metagenome sequencing data.

Dr. Ravi Kumar Chilukoti
Head – India Technical Support & PM, MGI, a member of BGI Group

Abstract

This talk will focus on DNBSEQ-G99ARS that is recently released into market by MGI which includes built-in Bioinformatics module and database of PFI (Pathogen Fast Identification) for ultra-fast identification of pathogens using metagenome sequencing data. This platform is ideal for small to medium sample volumes requiring Pathogen Identification by MetaGenomics/ATOPlex technology, WGS of small genomes, medium sized panels for target enrichment of Exome and Oncology samples. These solutions are being mentioned as “total solutions”, because MGI do provide all consumables and software solutions for sample to report.

Genomics India 2023

Capacity-building in genomic surveillance of infectious diseases in Peru

Dr Chakshusmathi Ghadiyaram
Mynvax Private Limited, Bengaluru, India

Abstract

Mynvax, a clinical stage vaccine biotechnology company, was founded with a singular vision of developing novel, improved, recombinant, thermostable vaccines for providing protection against respiratory viral infections. Founded in 2017, Mynvax uses its core capability of structure-based protein stabilization and engineering to design and develop novel vaccine antigens. These antigens are usually surface proteins of the target viruses, such as the hemagglutinin of the influenza virus and the spike glycoprotein of the SARS -CoV-2. Mynvax currently works on two major vaccine programs - a multivalent vaccine against the human influenza virus and a broadly protective vaccine against several variants of concern of SARS-CoV-2. Our novel recombinant engineered protein subunit vaccines are safe and efficacious and are entering human clinical trials in multiple geographies. Some of the ongoing work will be presented at the GIC2023 conference.

Genomics accelerated seed product development

Dr. Satish Kanuganti
Rallis India Ltd, Hyderabad

Abstract

Plant breeding combined with Genomics Technologies has been playing a key role in developing superior performance lines/hybrids with beneficial alleles for various biotic, abiotic and agronomic traits. This presentation will share a general overview on the genomics accelerated breeding for rapid seed product development. This presentation will also cover majorly genomic predictions-overview, advances, implementation and challenges for accelerated seed product development. Trait genetic complexity and intervention of genomics for breeding acceleration through various approaches will be shared. This presentation will benefit the plant breeding research community in terms of understanding complexity and deployment methods of genomics in breeding programs to develop superior lines or hybrids quickly.

Genomics India 2023

Cardiomyopathies – is there something beyond clinico-pathological features?

Pradeep Vaideeswar
Department of Pathology (Cardiovascular & Thoracic Division), Seth GS Medical College, Mumbai

Abstract

After ischemic heart disease, the other important subset of myocardial disorders is cardiomyopathies (CMP), which are characterized by structurally and functionally abnormal myocardium in the absence of abnormal conditions that would explain the observed dysfunctions. The important non-ischemic disorders under this group are dilated, hypertrophic, arrhythmogenic and restrictive CMPs with an approximate combined prevalence of 3 %. Importantly, many among them harbor mutations producing abnormalities in the sarcomeric or non-sarcomeric proteins with variable inheritance and penetrance. Though many of the patients present with recognizable (overt disease) clinical presentation, imaging characteristics and pathological features (usually biopsy or in rare instances myectomy), some unfortunate patients with covert disease die suddenly and form an important group within sudden cardiac death. The deceased are subjected to medico-legal autopsies and in such cases, apart from a detailed cardiac evaluation, it is important to harvest tissue for a molecular analysis of the underlying mutations. This provides an answer to the cause of death and also helps to identify relatives who may also harbor these mutations and may themselves be at risk for sudden deaths.

Genome dynamics of enteric pathogens with special reference to antimicrobial resistance

Niyaz Ahmed
Pathogen Biology Laboratory, School of Life Sciences, University of Hyderabad, Hyderabad, India

Abstract

The human gut presents a complex ecosystem harboring trillions of microorganisms living in close association with each other and the host body. Any perturbation or imbalance of the normal gut microbiota may prove detrimental to human health. Recent genomics-driven research, including some of our own studies has provided insights into the transmission and evolutionary dynamics of major enteric pathogens such as Escherichia coli, Vibrio cholerae, Helicobacter pylori and Salmonella spp. The next major challenge for public health epidemiologists is to understand the interactions and functioning of these pathogens at the community level, both in the gut and the outside environment. This is pertinent in the light of emerging antimicrobial resistance (AMR) being one of the immediate threats posed by pathogenic bacteria in the form of a multi-layered fitness advantage which manifests as phenotypic drug resistance at the level of clinics and field settings. To develop a holistic or systems-level understanding of such devastating traits, present methodologies need to be advanced with the high throughput techniques integrating community and ecosystem/niche level data across different omics platforms. This would provide new insights in to the dimensions of enteric bacteria in different environments and niches and would have plausible impact on infection control strategies in terms of tackling AMR.

Genomics India 2023

Determinants of Prakriti – a roadmap to personalized medicine

K. Satyamoorthy
Manipal School of life Sciences, Manipal Academy of Higher Education, Manipal-576104.

Abstract

Intrinsic heterogeneity of phenotypes and genotypes among individuals of a population influences traits, predisposition to diseases, treatment responses and disease outcomes. Ayurveda describes prakriti of an individual as basic elements of phenotypes that determines health and influences due to lifestyle practices, diseases, and treatment. These basic elements involve deduction of anatomical, physiological, and psychological features of an individual. The features are then classified into the combination of three doshas or body humors (Vata, Pitta, Kapha) to determine the prakriti of an individual, and any imbalances can indicate vikruti or disease states. Efforts are being made to integrate prakriti concepts into mainstream contemporary medicine for better health management. Large number of studies have been performed to provide a scientific basis for this traditional concept. These include biological, biochemical and molecular studies and in relation to diseases that have unearthed relationship to prakriti. Striking differences among the prakriti in genome wide studies such as for SNPs, transcriptome and DNA methylation have been reported suggesting that prakriti types have strong genetic and epigenetic basis. In addition, microbiome (oral and gut) and metabolomics studies have provided further evidence for prakriti specific distribution and predominance. Modern personalized medicine conceptualises an individual to be unique and thus their disease susceptibilities, and accordingly treatment modalities are tailored for every individual for effective outcome. Prakriti phenotypes embodies the Indian ayurveda system of ‘personalized medicine’ whose primary aim is to maintain health and prevent/eradicate diseases with a large emphasis on the knowledge of disease manifestation and its progression in relation to the host effects due to environment factors, lifestyle practices, dietary intake along with herbal and traditional medicines, making it highly personalized to the patient. The research performed in our laboratory on the genomic basis of prakriti will be presented.

Neurogenomics: Unraveling genic links to neurodegeneration

Dr Mohammed Faruq
CSIR-IGIB, New Delhi, INDIA

Abstract

Neurodegenerative disorders are a significant challenge in human history and it appears to remain so in the time ahead. Alzheimer, Parkinson disease and motor neuron disorders are causally heterogeneous and complex disorders and while some respite scientifically we observe tackling other spectrum of neurodegenerative disorders e.g. hereditary ataxias, hereditary spastic paraplegia and Chracot Marie Tooth disease. The latter group of disorders provide a window to look into the converging path of global neurodegeneration mechanistically. My group has dealt with unravelling monogenic aspects of neurodegeneration using a common screening protocol to the deployment of next generation tools. The hidden and unknown knowledge of neurodegeneration will remain the area of focus in the upcoming future and will be the focus of study for precision medicine.

Genomics India 2023

Gene therapy for an inherited eye disorder and mitochondriopathy

Dr.P.Sundaresan
Aravind Medical Research Foundation, Aravind Eye Hospital, Madurai-625020, Tamilnadu | Email ID. sundar@aravind.org

Abstract: Leber Congenital Amaurosis (LCA) is a genetically heterogenous disorder and cause severe visual impairment for infantile blindness. Currently 29 genes were implicated in the pathogenesis of LCA. However the clinical symptoms are very often similar to other retinal dystrophies, so the accurate clinical diagnosis, especially in infants, sometimes cannot be made at the first visit or has to be revised once the molecular analysis is performed. Genetic-molecular testing is necessary to obtain a definitive diagnosis of LCA through the identification of a pathogenic variant. Therefore, our study revealed the genetic etiology of south Indian LCA patients using panel-based targeted sequencing. Moreover, molecular diagnosis helps to understand the genetic etiology, which would further help to provide an accurate clinical diagnosis, genetic counseling and pave the way for gene therapy.

Leber Hereditary Optic Neuropathy (LHON) is a mitochondrial disorder that causes selective degeneration of retinoganglion cells due to bioenergetic failure of the electron transport complex I of the mitochondria. Mitochondrial complex I deficiency shows extreme genetic heterogeneity and can be caused by mutation in either nuclear-encoded genes or in mitochondrial-encoded genes. In 2020, our lab has conducted a hospital-based five-year prospective study on LHON and revealed only 43.6% of the affected individuals harbor primary mtDNA mutation. In addition, cybrid model was developed to understand the LHON pathogenesis.

In my talk I will explain in detail about these two ocular disorders (LCA and LHON). Gene therapy possibilities for LCA and LHON prevalence, screening, importance of primary mutations, functional studies and the clinical trial will be discussed.

Molecular survillence of antimalarial resistance from Indian P. falciparum isolates

Praveen Kumar Bharti
ICMR-National Institute of Malaria Research, New Delhi 110077, India

Abstract: The worldwide increase in malaria incidence and mortality since 2019 is challenging malaria control and elimination The emergence and spread of antimalarial drug resistance pose a major challenge to a successful malaria control program, particularly the containment of resistance to artemisinin-based combination therapies (ACTs), the first-line treatment against P. falciparum infections. Drug resistance is typically caused by a handful of mutations at particular genes in the parasite's genome. Mutations against sulfadoxine-pyrimethamine, at specific codons in the Pfdhfr (N51I, C59R, S108N, I164L) and Pfdhps (S436A, A437G, K540E, A581G and A613S/T) loci, which occurred in a particular order to gradually increase the level of drug resistance. Artemisinin resistance is mainly associated with mutations in the Kelch-13 propeller region.

Genomic DNA was isolated from blood samples collected from different malaria endemic region of India and sequenced for gene specific mutations using Sanger sequencing chemistry. A total of 1000 samples from 10 differnt sites were subjected to PCR amplification and sequencing. Among these, around 800 samples were successfully sequenced for each genes.

Double mutation (59, 108) in Pfdhfr gene was highly, followed single mutation S108N. Triple mutation (N51I, C59R, S108N) and Quadruple mutation (N51I, C59R, S108N, I164L) were only found in north east sites. In the Pfdhps, single mutation S436A was highly prevalent through out the entire country with variable prevalence. No functional mutations were found in Pfk13 gene. The finding suggested that India has not yet been found to have widespread ACT resistance.

Genomics India 2023

Nutritional security, Bio-security, Biodiversity perspectives in Sustainable development of Agriculture in India

Dr. M. S. Rao,
FNAAS, Campaigner of Sustainable Agriculture, Bangalore, India | 9480607571, 9482603614, msraobio45@gmail.com

Abstract: Sustainable development agriculture on healthy soils can only sustain the human race on this living planet in the future. Nutritional security, Bio-security, Biodiversity perspectives have to be considered in the development of strategies of Sustainable Agriculture in India. Bio-security & Biodiversity aspects of biologicals have assumed tremendous importance of late, as globalization and indiscriminate use of various agro-chemicals leading to excessive chemicalization of agriculture eco-systems. Serious reduction in the biological suppression of pests and pathogens due to injudicious use of agro-inputs resulted in to numerous hazardous effects on environment, plant, animal and human health.

The serious imbalances in beneficial microbiome in the soil dynamic life have been a concern of most of the researchers and policy makers in India and World.
This scenario has affected the sustainability of production systems which resulted in the increased cost of cultivation, inefficient use of agro-inputs and gradual decline in the yield levels in many crops.

Global climatic changes have been threatening the resilience of production systems everywhere demanding the researchers to standardize climate resilient-cost effective, eco-friendly sustainable protection and production systems not only for food security but also for the nutritional security in all the Nations across the Globe.

Efforts made by our team has led the maintenance of bio-diversity of soil microbiome in India during the last decade and paved the way for the sustainable agriculture through the use of various strains of bio-pesticides and biologicals and the details of which are going to be discussed in my presentation.

First draft Genome of Punica granatum L. 'Bhagwa'

Sushil Kumar Middha
DBT-BIF Facility, Department of Biotechnology and Biochemistry, Maharani Lakshmi Ammanni College for Women, Bengaluru, India

Abstract:
Punica granatum L. (Pomegranate) is a fruit-bearing deciduous shrub or small tree that belongs to the family Punicaceae. It is an antioxidant rich fruit and has been considered "apharmacy unto itself" by the Ayurvedic medicine. To gain insights into the complete metabolic potential of this plant whole nuclear genome was sequenced for the first time combining the sequence data from 3 libraries and two NGS platforms. The first draft genome assembly of Punica granatum L. 'Bhagwa' is a297.91 Mb. The transposable elements occupied 5.02% of the genome. and SSRS of Mono/di/tri/tetra/penta/hexa-repeats density in the genome was 491.7SSRS/Mb. In addition to SSR markers, 48203 proteins were identified. Phylogenetic analysis revealed Eucalyptus grandis as its nearest neighbor. Pathway analysis indicated an abundance of phenylpropanoids and Flavonoids in Punica granatum L. The genome sequence and gene annotations of Punica granatum L. offers new avenues of research into the function of genes and the phyto-pharmaceutical nature of the secondary metabolites. This genetic information is extremely pivotal for mining biosynthetic pathways, identify genes for disease resistance and improve the nutrition and yield.

Keywords- Bhagwa var., Nanopore, Pomegranate, Sequencing

Genomics India 2023

Genomics in India- a vanguard of modern healthcare: a tale of two diseases

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Abstract

Genomics is an emerging branch of modern medicine which involves assessing and interpreting regions of DNA that are likely to be associated with diseases. The technological prowess that genomics offers has led to tremendous healthcare benefits in all branches of medicine, from diagnostics to development of cutting-edge therapies. In this talk, I will describe two indigenously developed genomics technologies based on single molecule molecular inversion probes that has the potential to make a lasting impact in healthcare delivery in the field of oncology and rare disease diagnosis. The first example will showcase the utilization of this technology to carry out ultra-low-cost and high-throughput sequencing based microsatellite instability testing in solid tumours in order to detect the most common hereditary cancer syndrome called Lynch syndrome. I will show how detection of patients with Lynch syndrome offers opportunities of deployment of targeted surveillance and cancer chemoprevention programs such as regular aspirin intake. In the second example, I will showcase the ability to detect point mutations and single exon level copy number variants in a single assay to simultaneously diagnose 23 common lysosomal storage disorders in India. With the current diagnostic rate of 5% with biochemical assays, deployment of this technique offers opportunity for early diagnosis and treatment these rare diseases. For both assays, I will present data on their accuracy for mutation detection, cost-benefit analysis for their introduction in the Indian healthcare setting and their potential to save lives.

Genomics of female Infertility

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Fellowship of Clinical Bioinformatics at Tehran University of Medical sciences - Iran
PhD of Molecular Medicine at Tehran University of Medical Sciences – Iran

Abstract

Infertility is a global public health issue that affecting 10% of couples, with both female and male factors contributing to the problem. Female-related infertility accounts for approximately 40% of causes. The most severe phenotype of female infertility is premature ovarian insufficiency (POI), which is characterized by the cessation of ovarian function, even in women under 20 years old. Another distressing pregnancy disorder is recurrent pregnancy loss (RPL), defined as the failure of two or more clinically recognized pregnancies before 20–24 weeks of gestation. Our team’s current study focuses on identifying genetic causes of infertility in both males and females, specially those affected by POI and RPL. Families with at least two affected members were recruited and underwent whole exome sequencing (WES) to identify novel gene/genetic alterations associated with the phenotype. By recognizing genetic variations in patients, we were able to determine precise cause of the disease and design therapeutic strategies for personalized infertility treatment based on disrupted molecular pathways. The genetic diagnosis also allowed for genetic familial counseling and anticipated pregnancy planning for other members of families.

Genomics India 2023

Glimpses into the methylome of Plasmodium from Clinical isolates

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Abstract

Malaria, an acute febrile illness caused by the Plasmodium parasite, remains a global health burden. Recent advances in genomics have identified DNA methylation in eukaryotic cells as an essential epigenetic mark that regulates gene expression and stress responses. These expression patterns have been studied using several genome-wide profiling techniques. With the advent of Nanopore sequencing, a benchmark for long-read sequencing technology has been established to study the methylome profile. Several computational tools have been developed to detect DNA methylation from nanopore sequencing reads at single base resolution.

Whole genome nanopore sequencing from clinical isolates of Plasmodium has shown methylation marks at intergenic and exonic loci. This largely uninvestigated epigenetic layer may present new information which could influence strategies targeted towards the control of disease progression by malaria parasites.

SARS-CoV2 infection induces microbial dysbiosis in patients with COVID-19

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Abstract

The COVID-19 pandemic has affected people across the globe creating an epidemiologic crisis that has forced researchers to understand the cause and consequences of SARS-CoV2 infection. One of the research areas is to understand how microbial diversity in COVID-19 patients is affected by SARS-CoV2 infection. Several reports have indicated that bacterial diversity is affected by viral infections including SARS-CoV2. In the current study, we have carried out 16S rRNA (V1–V9 variable regions) gene sequencing of microbial DNA isolated from nasopharyngeal swabs (NP) and stool (gut) of COVID-19 patients using the Oxford Nanopore platform. We observed significant microbial dysbiosis in the NP and gut microbiome of patients with COVID-19. This dysbiosis was marked by an increase in the abundance of opportunistic pathogens in SARS-Cov-2 infected patients. The NP microbiome showed a significant abundance of Mycobacteria spp. and Mycoplasma spp. which suggested their possible role in co-infections in COVID-19 patients. The gut microbial population showed an enhanced abundance of opportunistic pathogens such as Cutibacterium, Corynebacterium, Clostridioides, and Enterococcus. Thus, our study indicates that SARS-CoV-2 virulence may promote the growth of opportunistic pathogens at both nasopharyngeal and gut microbiome levels, which may lead to co-infection or secondary infection in COVID-19 patients.

Genomics India 2023

SARS-CoV-2 genomic surveillance and immune evasion

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Abstract

Since the beginning of the pandemic caused by the novel coronavirus 2019, several new variants of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have emerged. The emergence of SARS-CoV-2 variants has impacted the infectivity, disease severity, treatment, therapeutics, diagnostics, and immunity both natural and induced. CSIR-NEERI has implemented the diagnostics of SARS-CoV2 along with whole genome sequencing to track the variants in the geographical area of Vidharbha in Maharashtra state of India. We have analysed the SARS-CoV-2 whole genome sequencing results of specimens collected across the Vidharbha region of India which encompasses 11 districts of Maharashtra during the year 2022. We found a diverse SARS-CoV-2 variant distribution which could be categorised into 54 pangolin lineages. These 54 SARS-CoV-2 pangolin lineages could be grouped into 12 clades. Notably, the most dominating variants belonged to Omicron B.1.1.529 (21.88%), BA.2 (43.94%), BA.2.75 (11.14%), BA.2.38 (4.8%), BA.2.12 (3.58%), and BA.2.10 (1.99%).

Considering the importance of monoclonal antibody (mAb) therapy for SARS-CoV-2 in immunocompromised cases, we also investigated the immune escape potential of the SARS-CoV-2 variants by mapping the amino acid substitution position in the spike glycoprotein RBD region.
We also investigated the coinfection dynamics of SARS-CoV-2 with H1N1-Influenza A in specimens collected across the Vidharbha region of India during the pandemic.

Integrated genomic surveillance - an era to leverage molecular technology to track existing pandemics and predict future ones

Mr Praveen KS
PATH South Asia hub

Abstract

A multisectoral integrated approach to surveillance is a key to identify potential outbreaks or future pandemics. Networking public health laboratories with the environmental department, animal health and agricultural department as a OneHealth is extremely essential to understand disease dynamics, given the risk of transmission between the various species. Block and District hospitals will be the key institutions to lead the surveillance activities from where routine sample will be collected. Identification of pathogens will be initiated and high-risk samples will be sent to Genome sequencing laboratories for the characterization of pathogens. Dissemination of the information will happen at State, National and International level for necessary planning and action. Post pandemic, the enhanced laboratory capacities at Block, District and Medical college levels would be of utmost importance to rollout the surveillance and adapt the use of genomic sequencing. Leveraging the use of available molecular technologies would be a game changer. It will be able to bring up more understanding towards the ability to detect and track outbreaks, identify risk factors and detect new infectious agents in a timely manner. Integrated genomic surveillance through use of molecular technology would be a pragmatic approach towards ensuring optimal health for people, animals and our environment.

Genomics India 2023

On the Genome and Transcriptome of Mycobacterium leprae; towards understanding genetic mechanisms of reactions and drug resistance in leprosy.

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Abstract

Mycobacterium leprae (*M. leprae*), the causative bacillus for leprosy, continues to infect endemic populations in tropical countries, with approximately 200,000 new cases of leprosy emerging each year globally. *M. leprae* infects the skin and the peripheral nerves causing skin lesions with loss of sensation resulting from demyelinating neuropathy as the bacilli infect the Schwann cells of the axonal myelin in the peripheral neurons. About 30-40% of leprosy-infected individuals in the borderline forms and rarely in the polar states manifest delayed-type hypersensitivity reactions, the type 1 reaction also known as reversal reaction, and the type 2 reaction known as Erythema nodusum leprosum (ENL). These inflammatory responses can occur before, during, and after the treatment with multidrug therapy (MDT) and are managed by immunomodulatory drugs in high doses that often contribute to morbidity.

Mycobacterium leprae transcriptomic and human host immune gene expression signatures that demonstrate a plausible association with type I (T1R) and type II reactions (T2R) aid in early diagnosis, prevention of nerve damage and consequent demyelinating neuropathy in leprosy. In our studies, the whole transcriptome expression array of these samples revealed significant overexpression of the genes that encode integral and intrinsic membrane proteins, hydrolases, and oxidoreductases. In T1R lesional skin biopsy specimens, the top 10 over significantly upregulated genes are ML2064, ML1271, ML1960, ML122, ML2498, ML1996, ML2388, ML0429, ML2030, and ML0224 in comparison to NR. In T2R, genes ML2498, ML1526, ML0394, ML1960, ML2388, ML0429, ML0281, ML1847, ML1618 and ML1271 were significantly upregulated. Predictive genomic, transcriptomic, and host immune biomarkers can play a critical role in detecting subclinical nerve damage and determining factors that trigger reactional states in leprosy.

On the other hand, antimicrobial resistance in leprosy is a growing concern that can hamper the efficacy of current multidrug therapy, which rely on the first-line drugs dapsone, rifampicin, and clofazimine, and the second-line drugs of ofloxacin, minocycline, and clarithromycin. Being a non-cultivable bacillus in the axenic media, *M. leprae* is propagated in the hind footpads of cross-bred albino mice. Use of both transcriptomic signatures and Whole genome sequencing of available mouse foot pad sensitive and resistant strains could reveal possible new mutation conferring resistance in leprosy. Comparative genomics of 154 genomes, among which 24 were from isolates resistant to one or more anti-leprosy drugs, and identified several hypermutated genes subject to positive selection, which we believe to play a role in drug resistance (fadD9, ribD and nth). While they are under characterization using surrogate mycobacteria, it's becoming essential to study the distribution of these mutations in drug-resistant and drug-sensitive strains. Newer sequencing technologies like the Oxford Nanopore Minion-based DNA sequencing system coupled with Biomeme qPCR device to amplify DNA, as a rapid drug resistance determining the protocol for leprosy in both lab-based and field-friendly settings, is in pipeline.

Genomics India 2023

Genomics in Forest Tree Breeding

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Abstract

Forest trees are still in an undomesticated state, harbouring a huge diversity of valuable alleles. Conservation of these forest tree genetic resources becomes utmost important to meet the future breeding goals. Forest tree improvement is just a few decades old, and it is a considerably more complex, time-consuming, and expensive enterprise compared to agricultural crop breeding. Even short rotation trees (e.g. Eucalyptus) can take 15–25 years to complete one breeding cycle. In India some of the plantation tree species like poplars, casuarina and eucalypts are cultivated in short rotation cycle to cater the needs of paper industries. But most of the timber yielding indigenous trees such as Melia, Gmelina, Teak, Pterocarpus and Dalbergia are grown under medium (minimum 20 years) or long rotation (minimum 40 years) cycles and demanding modern methods for assessment of genetic diversity and tree breeding. Recent developments in genomics have transformed traditional genetic improvement by introducing several types of molecular markers and advanced strategies to fasten the dissemination of quality planting material. Genome sequencing efforts in forest trees have surged due to high throughput sequencing technology and plunging sequencing costs. As a result, genomic selection approach is projected to be far more effective than traditional breeding for forest tree improvement. Further, to understand the functional genetic architecture of trees, -omic technologies are widely used.

Genomics based DNA fingerprinting is used in chain of custody to trace the origin/source of timber across a supply chain and prevent illicit timber harvesting in many countries that are sensitive towards deforestation and interested in responsibly sourced timber products. Timber origins to exact tree are always properly verified by DNA-based forensics, and broader genetic provenance testing methodologies reveal valid timber origins from the predicted plantation area. Population genetic structure indicates the genetic clusters present in a geographic location, allowing for the verification of the geographic origin.

Understanding and measuring adaptive genetic diversity in populations, as well as their reaction to climate change, is crucial for afforestation, seed source selection, forest management decisions, and gene resources conservation. Landscape genomics, in conjunction with geographic and environmental information, allows for the interrogation of genome-wide variation in order to understand the extent to which evolutionary forces shape past and contemporary population genetic structure, as well as to identify those populations that may be most vulnerable to future climate change. Assisted migration, through human interventions is one of the conservation measures to mitigate local adaptation, can be practiced with the knowledge on population genomics. Neutral and adaptive regions of the genome can be determined and there by identify suitable seed sources and delineate genecological zones to help assisted migration and conservation of forest genetic resources. Current results suggest that genomic applications in forestry have excellent potential for strengthening genetic improvement and conservation of genetic resources.

Genomics India 2023

Analysis of genetic diversity and identification of genome-wide markers associated with foliar disease resistance in Para rubber (Hevea brasiliensis)

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Abstract

The Para rubber tree (*Hevea brasiliensis*) is the major commercial source of natural rubber in the world accounting for 99 percent of the world's total natural rubber production. However, the improvement in rubber productivity is greatly affected by the availability of narrow genetic base for exploiting breeding potentials, difficulty in introducing wild germplasm due to linkage dragging of unfavorable alleles and susceptibility to a broad range of pathogens and pests that cause significant economic loss.

A panel of 116 individuals used in the diversity analysis, consisted of 110 clones from *H. brasiliensis* (54 from Malaysia, 51 from India, five from Sri Lanka, four from Indonesia and two from China), one representative from each of *H. benthamiana*, *H. camargoana*, *H. pauciflora*, *H. spruceana* and *H. nitida* and an interspecific hybrid FX 516. A phylogenetic tree was constructed using genome-wide single nucleotide polymorphisms (SNPs) developed from a next generation sequencing platform at Diversity Arrays Technology, Australia.

According to the phylogenetic relationships revealed from 12,078 SNPs, clones from different countries grouped together and clones that shared a common parentage from different countries clustered together. Although all cultivated rubber derived from a narrow genetic base, founder effects detected from seedlings from different countries would provide opportunities for expanding the genetic basis and breeding potentials, understanding the population structures and for determining the degree of evolutionary divergence in rubber.

An integrated linkage map for an F1 progeny of 86 from an interspecific cross between *H. brasiliensis* and *H. benthamiana* using 23,978 markers [10,323 SNPs and 13,655 SilicoDArTs], spanned 3947.83 cM with 0.83 cM average marker-interval. Marker-trait association analysis was conducted for the diseases caused by major pathogens of rubber: *Phytophthora* spp., *Corynespora cassiicola*, and *Colletotrichum* spp and identified 12 significantly associated SNPs in six linkage groups: 2, 6, 12, 14, 17, and 18. Kompetitive Allele-Specific PCR marker assays were developed for those 12 SNPs to be used in marker-assisted breeding in rubber. Within the proximity to those SNPs, 41 potentially key genes that have previously been reported to associate with plant disease resistance were predicted with high confidence.

Genomics India 2023

Advanced computational approaches for chromosome-scale haplotype-resolved genomics

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Abstract

Reconstructing the complete phased sequences of every chromosome copy in human and non-human species are important for medical, population and comparative genetics. The unprecedented advancements in sequencing technologies have opened up new avenues to reconstruct these phased sequences that would enable a deeper understanding of molecular, cellular and developmental processes underlying complex diseases. Despite these interesting sequencing innovations, the highly polymorphic and gene-dense regions human leukocyte antigen (HLA) are not yet fully phased in the reference genome. The reference genome still contains gaps in multi-megabase repetitive regions, and thus annotating novel expression and methylation results are incomplete and inaccurate, that affect the interpretation of molecular genetics and epigenetics of diseases. There is a pressing need for a streamlined, production-level, easy-to-use computational approaches that can reconstruct high-quality chromosome-scale phased sequences, and that can be applied to hundreds of human genomes.

In this talk, first, I will present an efficient combinatorial phasing model that leverages new long-range Strand-specific technology and long reads to generate chromosome-scale phasing. Second, I present an efficient algorithm to perform accurate haplotype-resolved assembly of human individuals. This method takes advantage of new long accurate data type (PacBio HiFi) and long-range Hi-C data. We for the first time can generate accurate chromosome-scale phased assemblies with base-level-accuracy of Q50 and continuity of 25Mb within 24 hours per sample, therefore, setting up a milestone in the genomic community. Third, I will present the generalised graph-based method for phased assembly of related individuals. This graph framework provides a compact representation to encode various data types and can be applied to genomes of any complexity having varying heterozygous rates and repeat content. Finally, I will present the importance of haplotype-resolved assemblies to various medical applications including cancer genomics.

In summary, my works efficiently and robustly combine data from a variety of sequencing technologies to produce high-quality diploid assemblies. These computational methods will enable high-quality precision medicine and facilitate new and unbiased studies of human (and non-human) haplotype variation in various populations which are currently goals of the Human Genome Reference Project.

Genomics India 2023

STUDENTS & DELEGATES ABSTRACTS

NEARLY THREE DECADES OF GENOMICS - LOOKING BACK & MOVING FORWARD

Genomics India 2023

Machine Learning-Based Ranking of Novel ALS-Associated Gene And Molecular Analysis of Identified Gene Candidates In Drosophila And IPSC Based 3D Cellular Models

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Abstract

The most common underlying cause of ALS is genetic mutations. With the rapidly evolving genomic technologies, large sets of ALS genome data are available for analysis. Over the years, because of numerous research, many genes linked with ALS have been identified but the list is continuously expanding. In one part of this project, machine learning-based approaches were used to analyze genomic data from249 people (27 are control subjects and the rest are ALS-positive) with various genetic backgrounds. Models were developed for identifying genes and SNPs associated with ALS. Models were trained to find unique ALS-linked genes or SNPs and further gene ontology enrichment, gene annotation and gene interaction analysis were performed. In parallel, we intend to study the effect of a few gene candidates from the above list in iPSC-derived neurons. At the same time, we also plan to parallelly perform a GWAS study in the Indian population from the data available through GenomeINDIA. A set of ALS-associated gene candidates would also be selected from this Indian population and its effect on ALS pathogenesis would also be analyzed using iPSC-derived neurons.

Independent of the genomics, we also have designed a novel genome-wide screen to identify genetic modifiers of ALS using suppressor and activator CRISPR screens in drosophila models and iPSC-derived neurons. We anticipate identifying several ALS modifier genes that will be further used for detailed mechanistic studies. With initial studies on 2D models, we intend to use the 3D brain organoids to study the pathological features of neurodegenerative diseases with respect to the identified genetic modifiers and explore the possibilities of targeting these genes for therapeutic applications.

Genomics India 2023

IN-SILICO INTERACTION OF TRIFLUMEZOPYRIM AND REPRODUCTIVE GENES OF A MODEL FISH , DANIO RERIO

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Reproductive genes are considered to be the important factors, enhancing the process of reproduction in living organisms. Sex steroids play an important role in gonadal development and gametogenesis. One of the vital genes associated with steroidogenesis is aromatase (Cyp19), which helps in conversion of androgen to estrogen. The fish aromatase is coded by two set of specific genes, the gonad-specific cyp19a1a and brain-specific cyp19a1b. Kisspeptin, is a neuropeptide, encoded by Kisspeptin1 (KISS1) gene, that primarily acts as a regulator of reproductive functions in vertebrates. However, with the increasing cases of water pollution, aquatic habitat is getting negatively affected, causing unwanted changes in aquatic organisms. Amongst the different factors contributing towards water pollution, agrochemicals top the list. Triflumezopyrim (Pexalon), is a novel mesionic pesticide, and is the supposed inhibitor of Brown Planthopper (BPH). In-silico assessment provides a platform to evaluate the effect of potential toxic molecule, against the molecular target. Molecular docking is a key tool, which predicts the preferred orientation, affinity and interaction of a ligand in the binding site of a protein. To understand the effect of triflumezopyrim on kisspeptin and aromatase, an in-silico assessment was performed, at the protein level. The protein tertiary structure, of both kisspeptin1 and Cyp19a1a, was downloaded from Modbase database and was validated using SAVES server. The PDB structure of triflumezopyrim, was generated from Pubchem database. Molecular docking was performed for kisspeptin1 and cyp19a1a as the major receptors and triflumezopyrim, as major ligand using SEAMDOCK server.The resulted docking conformation in case of kisspeptin1, the lowest binding energy was found to be -8.0 kcal/mol. There were a total of thirteen atom contacts found between the ligand and the protein. Triflumezopyrim interacted with three amino acids forming hydrogen bond with Leu40, Glu84 and Asp85. Apart from the hydrogen bonds, Leu37, Val39, Val86, Val89, Leu59 contributes to hydrophobic contact, Arg83 is a major contributor of cation-pi interaction and Asp85 corresponds to weak hydrogen bond. The docking conformation in case of (Cyp19a1a), the lowest binding energy was found to be -9.7 kcal/mol. A total of eleven atomic contacts were found between the ligand and the protein. Triflumezopyrim interacted with only one amino acid forming hydrogen bond with Pro251. Ten out of eleven interactions were found to be hydrophobic contacts, which includes Val79, Ile90, Ile101, Ile109, Thr114, Pro251, Phe391,Arg394, Asp412 and Ile414.This ligand-binding interaction alters the conformation of the receptor, as it affects the three-dimensional shape orientation. This in-silico hypothesis, that shows the binding activity, paves way to conduct in-vivo and in-vitro investigation ,to understand theimpact of triflumezopyrim, over kisspeptin1 and cyp19a1a activity in vertebrates.

Keywords- Agrochemicals, Brown Planthopper, molecular docking, triflumezopyrim, steroidogenesis.

Genomics India 2023

Study of Vaginal Microbiome by Metagenomics Approach.

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Abstract

In present work, an attempt was done to study vaginal microbiome by culture based and culture independent study by metagenomics approach. There are different factors affecting the vaginal health such as gynecological cancer, menstrual cycles, pregnancy. Individual women ‘s lifestyle also affect the vagina health as their sexual activities their way of living their diet etc. all these factors are important to maintain vaginal health, but this generation don’t not really focus on their lifestyle and diet with has increased more cases of vaginal health. We have collected the vaginal samples from various healthy women and studied then at both level culture dependents and independent. Culture based study found that there were 11 morphologically and biochemically different isolates, with having good antimicrobial activities. These recent advancement in the culture independent method has made the analysis easier as earlier some of the microbes couldn’t be culture hence were not studied. using this culture independent method of molecular analysis has produced an explosion in studying human bacterial microbiota in various ecosystem. Applied to the human vaginal ecosystem, these molecular methods have shown the presence of a very important proportion of uncultivable bacteria in the vaginal econiche. Various metagenome analysis tools were used to analyzed the sequence data, and we determined that the samples had large dominance of *lactobacillus* spp. as when they studied thy also had normal vaginal flora is dominated by various species of *Lactobacillus*. And the other species was Firmicutes; we could also analyze other phylum Domaine order genus etc. we found that had 5 domain, 9 kingdom, 92 Phylum, 169 classes, 315 order, 607 family ,1248 genus and 2535 species. From all the study of metagenomic we could find that the normal vaginal sample was dominated by *lactobacillus* species that would protect the vagina by maintain the ph. between 3.5 – 4.5. Dominant presence of this *lactobacillus* spp indicated the healthier vaginal flora. This work may lead to improved diagnostic tools and treatments for women who suffer from, vaginal imbalances, pregnancy complications, and sexually acquired infections.

Keywords: Metagenome, Microbiome, *lactobacillus,* vaginal

Genomics India 2023

High-throughput Comparative Genomics and Machine Learning-Based Classification of Escherichia coli Sequence Types - Implications and New Findings

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Abstract

Over the past two years, the entire world has witnessed the global threat posed by the COVID-19 pandemic. Well before COVID-19, we have been living through a growing global threat of antimicrobial resistance (AMR), which has not been given as much attention as COVID-19. If the situation remains the same, AMR is expected to claim more than 10 million lives each year by 20501, making it the leading cause of fatalities. On the evolutionary timescale, horizontal gene transfer (HGT) mediated acquisition of genomic fragments, chromosomal reduction, and genome optimization has played an important role in shaping the bacterial genome to survive environmental vulnerabilities2. As a result, the natural residents of the gut mucosa, such as E. coli (commensals) have evolved into different pathotypes/sequence types (STs), posing a serious threat to the current treatment regimens. The medical interventions against these pathogens are further complicated/delimited by the emergence of multidrug-resistant (MDR) strains and the lack of efficient drugs in the drug discovery pipeline. Hence, it is very pertinent to understand the key molecular mechanisms underlying the evolution and dissemination of these MDR superbugs. As a part of our study, we analyzed a compendium of 5,653 E. coli genomes representing 19 different STs (including both well-researched and understudied STs) using supervised machine learning algorithms, with Random Forest Classifier and Extra Trees being the best-performing algorithms. The high-throughput comparative genomic analysis revealed significant diversity in terms of their genomic features (AMR genes, virulence genes, mutations, integrons, Transposons, and plasmids) across 19 STs. Furthermore, this study provides initial working evidence regarding the clonal evolution of E. coli. Machine learning-based predictive modelling identified 86 key ST-specific signatures belonging to different protein superfamilies, including toxin-antitoxin (TA) systems, that could be implicated in context-specific adaptation strategies, including drug tolerance3. Further, we are trying to understand the link between the pathogenic attributes and TA systems in the evolution of E. coli STs. Some of these ideas and our latest findings and proposals are summarized herein.

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Genomics India 2023

A comparative study on the detection of M. leprae DNA in urine samples using Rlep PCR with the other conventional clinical samples in treated and untreated groups of Leprosy.

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Background: Leprosy is a chronic and highly stigmatized infectious disease caused by Mycobacterium leprae. For the identification of M. leprae in clinical samples only some diagnostic tools such as bacillary load, a histopathological analysis is used. The diagnosis in leprosy has been quite challenging especially in paucibacillary cases. In this scenario, PCR is being used as an effective tool for the detection of M. leprae DNA using different gene targets/markers in various clinical samples. Among all the different gene targets, Rlep gene (Repetitive element) was found to be most sensitive and specific to M. leprae detecting even minute quantities of DNA. The present study aims to detect M. leprae DNA in urine samples, which is very easily available and non-invasive sample using PCR with Rlep gene, in treated and untreated leprosy patients. The PCR result was compared with the invasive samples such as blood and slit skin smears and among treated and untreated groups of Leprosy.

Materials and Methods: A total of 91 samples were enrolled in the study. Blood, urine and slit skin smear samples were taken with informed consent form. Among which 76 were leprosy patients and 15 control were included. DNA extraction and Rlep PCR were performed in all these samples.

Results: Among the leprosy cases PCR was positive in 56.6% in urine samples, 51.32% positive in Smear samples and 42.1% in blood samples. Among the control group all 15 samples showed negative PCR in urine, smear and blood samples. The PCR positivity showed 65.6% in urine samples of untreated group and 31.5% in urine of samples of treated group.

Conclusion: Although no significant difference was seen between the PCR positivity in smear and urine samples, Urine PCR still could be useful for diagnosis in leprosy patients and to check subclinical infection in household contacts as its noninvasive method of sample collection. Further studies are needed to evaluate the above study with a large number of patients.

Genomics India 2023

PHYSICOCHEMICAL CHARACTERISATION OF PROMOTERS USING MOLECULAR DYNAMICS SIMULATION BASED PARAMETERS

Presented by: Dinesh Sharma (IIT Delhi, run478@gmail.com, 07042143919)

Abstract or Summary - Recruitment of RNA polymerase (RNAP) to specific transcriptional start sites (TSSs) has remained a mystery because prokaryotes and eukaryotes have nearly no consensus promoter sequence. Understanding the fundamental mechanism is essential to comprehending the idea of gene regulation. Working with the hypothesis that genomic DNA sequences must convey their functional roles through their physico-chemical properties, we have characterized, in this study, the promoter regions (of prokaryotes and eukaryotes) using molecular dynamics simulation derived structural and energy parameters over all the possible unique trinucleotides and tetranucleotides. These physico chemical properties (28 properties) show distinct signatures at the TSS.

Short Introduction - Over the years, scientists have constantly been working to develop various computational algorithms for the annotation of promoters. Promoters are one of the genome's most essential components. These elements commence the transcription process by primarily binding to the RNAP. The promoter's function, however, is not restricted to transcription start. These regions aid in appropriately identifying and confirming predicted genes in genome annotation. Having no universal approach for their efficient characterization. The present biophysical outlining distinctly delineates the TSS in both prokaryotes and eukaryotes by mapping the physico-chemical characteristics on the trinucleotide and tetranucleotide steps. These increased nucleotide steps incorporate neighbouring effects from the adjacent nucleotide and have provided us with new insights into the structure and energetics of DNA, different from the dinucleotide-based characteristics.

Aims and Objectives – Our objectives include calculating the 25 structural parameters through μ second MD simulations and three energy parameters through in-house software. These parameters were used to profile TSS from prokaryotes and eukaryotes and were compared to the consensus at TSS sites in both the areas. Further we validated the evidence of characteristics on individual sequences.

Methodology - Structural profile of DNA was defined by 25 parameters belonging to Base-Pair Axis, Backbone, Inter-Base Pair, Intra-Base Pair. For the energetic profile, we relied on Hydrogen-bonding, Stacking and Solvation Energy. These parameters were used for the profiling of 16,519 transcriptional start sites from 12 prokaryotic organisms and 197,356 TSS from 8 eukaryotic organisms (yeast) and have made a comparison with the consensus profile of the same. To further explore the granularity of the signal trend in individual sequences, a threshold analysis was done.

Results and Discussions - Our results firmly convey the idea that DNA uses the same dialect for prokaryotes or eukaryotes and that it pays to go beyond sequence level analyses to physico-chemical space to elicit functional destiny of DNA sequences. DNA elements through their structural and energy profiles communicate similarly for both prokaryotes and eukaryotes suggesting universality of DNA language.

Conclusions - Our analysis reveals that while sequences may show variations at TSS within the DNA, the structure and energy profiles imparted by these sequences are always conserved.

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MOLECULAR ENDOCRINE MODEL MECHANISM OF INSECT METAMORPHOSIS AND JH ACID AS THE KEY RESISTOR

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Abstract

Metamorphosis comprises dramatic transformation in shape and function of organs, tissues and individual cells. According to the classical theory of the hormonal control of insect metamorphosis, ecdysteroids initiates a molt independent on the titer of JH.However a few observations earlier indicate that tissues must first acquire competence in the presence of JH acid alone is not sufficient for the metamorphic response to ecdysteroid. JHacid is an inactive precursor and metabolite of JH actually induces cells to become competent to undergo metamorphosis, whereas ecdysteroid merely stabilizes this commitment and facilitates the expression of this state of development program.The model system used in this project is the common mormon butterfly Papillio polytes is a major pest of Rutaceous plants. Metamorphosis especially molting behaviour in insects is known to be governed by specific dermal glands known as Verson's glands.Ecdysteroid induces and coordinates the molting process and JH determines the nature of moult. JH acid is an inactive precursor and metabolite of juvenile hormone (JH) that induces cells to become competent to undergo metamorphosis, whereas ecdysteroid merely stabilizes this commitment that facilitates the expression of this state of developmental programme. Verson's glands that are found specifically in lepidopteran insects are paired dermal glands of epidermal derivatives which contribute a protective layer to the newly formed cuticle or might has defensive function. These glands are of particular importance because specific protein products from both larval and pupal stages can be made simultaneously by this glandular cell in the midst of this transition. In Papilio polytes these glands are present in pairs on the antero-dorsal region of each segment lying immersed in the epidermis. In the present study localization of Verson's glands in the lepidopteran, Papilio polytes were done to analyze secretory pattern and protein profile of the Verson's gland protein (VGP) during the insect developmental cycle. The specific role of JH metabolite, the JH acid in the induction of metamorphic competence were examined. Elucidation of the fundamental mechanism and interaction of insect endocrine molecules during insect metamorphosis were also explained.

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MUTATIONAL HOTSPOTS AND SIGNALLING NETWORKS ASSOCIATED WITH THYROID CANCER

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Abstract

Thyroid Cancer (TC) is the most prevalent endocrine malignancy that develops in butterfly-shaped thyroid gland which produces thyroid hormones responsible for metabolism, weight, blood pressure, heart rate, body temperature.TC leads to hoarseness, sore throat, and lumps. Like other cancer types, TC is also caused by genomic abnormalities with a few well-studied TC driver genes which are frequently mutated. However, many infrequently mutated genes may also contribute to TC progression and malignancy. Hence, this study of TC genes, their mutational profiles and pathways associated with TC. In this study, we collected 5,979 TC genes from four TC studies containing 1,629 samples of 1,620 patients in cBioPortal. We analysed mutational frequency of TC gene, pathway enrichment, role of mutations in various signalling pathways, and compared our gene list with TC panels. We analysed TC gene enriched pathways (n=25) with admissible combined score and P-value. We found 10 genes, which are frequently deregulated cancer pathways. We identified RTK/RAS and Wnt pathways possessing a higher number of genes mutated in TC. We compared our TC gene lists with genes used in TC panel studies and we found that 6 genes (CDC73, PRKAR1A, RET, SDHB, SDHD and SRGAP1) with low frequency of somatic mutations but due to germline mutations in these genes are part of the TC panels as deduced from hereditary TC studies. All in all, this study provides an insight into the mutational spectrum of TC genes and their association in signaling pathways.

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Deep sequencing based RNAseq analysis of luminal-B like (Her2 positive) breast cancer in Indian women

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Aim/objectives
Breast cancer is one of the major diseases affecting Indian women. The main objective of this work is to identify important candidate genes and functional pathways associated with luminal-B like (Her2 positive) breast cancer in Indian women using deep sequencing based RNAseq analysis of transcriptomes of tumor and surrounding tissues.

Methods
Tumor and adjacent Tissues were obtained from patients with luminal-B type (Her2 positive) breast cancer. RNA was isolated from these samples, and the transcriptomes were sequenced using Illumina technology at Genotypic Technologies, Bengaluru. The paired-end raw reads were pre-processed using cutadapt tool. Transcripts differentially expressed between the tumor and surrounding normal tissue samples were identified using reference-based assembly. Reference based assembly of pre-processed quality reads from all samples was carried out using HISAT2, a splice aware aligner. The reads were mapped on to the human reference genome (GRCh38) sequence as reference. Read count normalisation and differential expression analysis was carried out using DESeq2, which detects differential expression by use of negative binomial generalized linear models. Functional annotation was done using clusterProfiler to identify the biological functions and important pathways in breast cancer. Protein-Protein Interaction (PPI) networks were constructed using Cytoscape tool. Expression data downloaded from TCGA was used to validate the expression pattern of selected genes.

Results
Differentially expressed genes were identified, and among the top significant differentially expressed genes that were dysregulated were cell cycle regulators, tumor proliferation markers and oncogenes. Functional enrichment analysis of DEGs revealed Important pathways associated with luminal B like (Her2 positive) subtype of Breast cancer in Indian women. Important hub genes were identified by PPI network analysis.

Conclusions
In this study, using deep sequencing of transcriptomes, identified key genes involved in luminal-B like (Her2 positive) breast cancer, which may open new avenues in diagnosis and treatment of breast cancer.

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TRINUCLEOTIDE AND TETRANUCLEOTIDE BASED UNIQUE STRUCTURAL AND ENERGETIC PROFILING AT INTRON-EXON BOUNDARIES

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Abstract or Summary - In eukaryotes, analysis of the location and structure of genes requires accurate exon-intron boundary detection. Due to weak consensus sequence and training restrictions on the experimental data sets that are currently available, the methodology for genomic signals that distinguishes exon and introns in a genome appears to be insufficient. Here, we introduce a novel idea for identifying exon-intron boundaries in genomic segments based on their structural and energetic characteristics. In this study, the exon-intron boundary regions have been characterised using molecular dynamics (MD) simulation derived structural and energy parameters over trinucleotide and tetranucleotide DNA steps. Our research clearly communicates the presence of signatures in the physico-chemical space for the exon-intron boundaries. These intrinsic signals based on tri and tetra nucleotides studied here appear to be more robust and stable.

Short Introduction - Eukaryotes are complex organisms having a membrane bound nucleus and cell organelles. In these organisms, a gene is composed of two essential elements, viz., introns and exons. Introns are the noncoding regions of a gene (or mRNA) that are removed before the maturation of the mRNA through a process called splicing. The segments of the DNA (or mRNA) that finally becomes part of the mature mRNA and thus code for the proteins are exons. Detecting accurate intron-exon architecture within a gene is essential and has recently received the utmost attention in eukaryotic genome annotation. Since there exists no universal model for the identification and characterization of exon-intron boundaries, the need of the hour is to come up with a chemistry-based approach to annotation. To come up with a universal approach we have investigated the structural and energy profile of the transition of intron to exon and exon to intron.

Aims and Objectives – Calculation of structural and energetic parameters using MD Simulation and in-house software, respectively. Physico-chemical profiling of intron-exon junctions using derived parameters. Individual sequence analysis using statistical tests.

Methodology - We have monitored the physico-chemical profiles using 25 structural parameters and 3 energetic features on 328,365 exon start/end sites from human genome. These profiles were compared with the various tri, penta and undecamer consensus motifs occurring at the junctions. To explore the granularity of the signal trend in individual sequences, a threshold analysis was done.

Results and Discussions - The structural and energetic profiling of exon-intron boundaries revealed unique signatures for the exon start and end sites. The consensus at the intron-exon junctions is poor. At these boundary junctions, DNA is rather seen to take on a unique structural and energetic state irrespective of the sequence.

Conclusions - The intrinsic signals obtained at intron-exon junction can assist in efficient identification and confirmation of these sites. The outcome of this study is likely to lead to a universal, robust, and highly sensitive physicochemical property-based method for characterization of intron-exon. These patterns in future could be utilized for designing improved genome annotation tools.

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Targeting the nucleocapsid protein of SARS-CoV-2 and FCoV for anti-coronavirus drug discovery

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Abstract:

SARS-CoV-2 and feline alphacoronavirus (FCoV) cause serious viral illnesses in humans and cats, respectively. The effective treatment strategy for the coronavirus infections with immunopathological complications such as SARS-CoV-2, MERS and FCoV are focused on antiviral and immunomodulatory agents to inhibit virus replication and enhance the protective immune response. Here we report the binding and conformational alterations in the nucleocapsid protein of SARS-CoV-2 and FCoV by a novel compound K31. K31 noncompetitively inhibited the interaction between the purified nucleocapsid protein and synthetic 5’ terminus of the viral genomic RNA in vitro. K31 was well tolerated by cells and inhibited the replication of both SARS-CoV-2 and FCoV in cell culture with a selective index of ~ 115. A single dose of K31inhibited virus replication to an undetectable level in 24 hours post-treatment. K31 did not affect the virus entry to the host cell but inhibited the post-entry steps of virus replication. The nucleocapsid protein forms ribonucleocapsid in association with the viral genomic RNA that serve as template for transcription and replication of the viral genome. Our results show that K31 treatment disrupted the structural integrity of ribonucleocapsid in virus infected cells. After COVID19 pandemic most of the antiviral drug development strategies have focused on RdRp and proteases encoded by the viral genome. Our results have shown that nucleocapsid protein is a druggable target for anti-coronavirus drug discovery.

Genomics India 2023

Understanding epigenetic changes in depression brains : Challenges and excitements

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Abstract:

The disclosure of the double helical structure of DNA by Watson and crick in 1953 have laid the ground work to all the scientist for further research work . Depression is one of the overlapping in many brain disorders. Depression is coupled as part of Bipolar disorder, which contact manic and depression in sequential form. The major identification of genome in a depression brain was observed as chromatin looping, epigenetic changes and gene alterations . My major focus is to understand the epigenetic changes like DNA methylation ,histone modification , and non- coding RNA action in a depression brain. The brain is considered as major organ and to understand it is a major task for now. Only 20% of the brain biology is understood making neurobiology implications more complex and leading to the cause of degenerative disorders like dementia , alzheimer's , parkinson's disease. In recent evidences epigenetic mechanisms such as DNA methylation, microRNAs, and histone modifications play a key role in psychiatric diseases such as depression. Depression not only alter the DNA sequence but also the way cells generate the energy. Almost 178 genes variants are responsible for major depressive disorders. Does these disorders leads to self-slaughtering conceptions-still a debate?. My current hypothesis, Chromatin under goes changes in depression leading to over expression or suppression of genes coupled with epigenetic changes.

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HESPERETIN MODULATES TGFβ INDUCED METASTATIC POTENTIAL OF PROSTATE CANCER CELLS BY ALTERING HISTONE METHYLATION MARKS

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Abstract

Prostate cancer is the most prevalent cancer in males, and usually, death occurs due to bone metastasis. TGFβ has been shown to play an essential role in the metastasis of prostate cancer cells by promoting epithelial-to-mesenchymal transition (EMT). Hesperetin is known to possess anti-microbial, anti-fungal, antioxidant, and anti-cancer properties and good bioavailability. This study investigated the effect of hesperetin on TGFβ-induced cell proliferation and EMT in prostate cancer cells. We found that hesperetin can significantly inhibit the cell proliferation of PC3 cells and arrest them in the S and G2M phases of the cell cycle. The invasion and migration assay results decipher the inhibitory effect of hesperetin on TGFβ-induced invasion and migration of prostate cancer cells. Hesperetin inhibits the canonical signaling pathway, as we observed a significant decrease in the expression of pSmad3. It inhibits the TGFβ-induced EMT by increasing E-cadherin expression and decreasing N-cadherin expression and also modulates TGFβ-induced histone methylation marks.

Introduction: Phytochemicals have been important chemopreventive and chemotherapeutic agents for the last decades. The reason for the failure of many phytochemicals in clinical studies is their poor bioavailability. To overcome that, one can explore the metabolite of the phytochemicals, which have extended bioavailability than the pure compound. Hesperetin is one such metabolite of hesperidin, a citrus flavanone. High-grade malignancies in cancer are caused due to a combination of processes; epithelial-to-mesenchymal transition (EMT) is one of them. The TGFβ-signalling pathway is renowned for inducing EMT during cancer progression. Therefore, in our study, we used TGFβ to induce invasiveness of prostate cancer cells and were interested in exploring the effect of hesperetin on TGFβ-induced invasion and migration of PC3 cells. We also studied the effect of hesperetin on H3K4me3, H3K9me3, and H3K27me3, in the PC3 cell line.

Materials and methods: MTT-assay, Cell-cycle Analysis, Wound-healing Assay, Western Blot analysis, Invasion Assay, RT-qPCR

Results: Hesperetin disrupted PC3 cell morphology and decreased cell viability. It arrested PC3 cells in the S and G2M phases of the cell cycle. It significantly reduced migration and invasion of TGFβ-induced PC3 cells. It inhibited the canonical TGFβ-signalling pathway and EMT. The trimethylation of H3K4 and H3K27 was increased after Hesperetin treatment. The H3K9me3 levels were increased in the presence of hesperetin alone but decreased when hesperetin was given after TGFβ induction.

Discussion: Phytochemicals are proving to be promising therapeutics against cancer. They are easily available, affordable, and have lesser side effects. This study also shows the epigenetic modulation of cancer cells by hesperetin, thereby opening new insights into the mechanism of action of phytochemicals.

Conclusion: Conclusively, our study found hesperetin as a promising future candidate against prostate cancer.

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In silico genome analysis to reveals the prolific antagonistic potential of Bacillus velezensis ZBBT5 and Bacillus licheniformis ZBHT4 against Meloidogyne incognita

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Abstract:

Spore forming Bacillus species are widely used as biocontrol agents against parasitic nematode infested crops in fields. However, information on genetic basis of their nematicidal action is obscure. Therefore, the present investigation was undertaken to elucidate the possible virulent determinants for two chitinolytic soil isolates viz. Bacillus velezensis ZBBT5 and Bacillus licheniformis ZBHT4 through its genome analysis. Genome annotation of Bacillus velezensis ZBBT5 (4.006 Mbp) and Bacillus licheniformis ZBHT4 (4.376 Mbp) revealed the presence of various genes responsible for plant growth-promoting activities such as root colonization, swarming motility, exopolysaccharide biosynthesis, chitin utilization, etc. Presence of genes encoding nematode-virulent proteases, chitinases, secondary metabolite biosynthetic clusters, toxic peptides like bacillomysin, lipopeptides like fengycin and iturin, strengthen their prospect of being used against nematode. The nematicidal activity was further confirmed by In-vitro tests which demonstrated that both the strains exhibited >60% mortality of the second stage juvenile and significantly inhibition of egg hatching when compared to untreated sets. Based on the findings, we propose Bacillus velezensis ZBBT5 and Bacillus licheniformis ZBHT4 as a model for screening biocontrol agents against root knot nematode Meloidogyne incognita.

Keywords:
Comparative genomics, Biocontrol agents, Bacillus spp. Root knot nematodes, virulence factors, etc

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A genetic analysis of early-onset Parkinson's disease in a cohort of Indian patients

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Abstract

Background:
Parkinson disease (PD) is the second-most common neurodegenerative disorder that affects 2–3% of the population ≥65 years of age. Neuronal loss in the substantia nigra, which causes striatal dopamine deficiency, and intracellular inclusions containing aggregates of α-synuclein are the neuropathological hallmarks of Parkinson disease. Approximately 10-15% of PD patients are diagnosed with early-onset Parkinson's disease (EOPD) with disease onset before 50 years of age. Hereditary component plays major role in EOPD as compared to late-onset PD (LOPD).

Objectives: We aim to identify potentially pathogenic genetic variants causing EOPD using next generation sequencing methods.

Methods: We collected blood samples from the patients which were diagnosed with PD and disease onset below 45 years of age. All patients underwent detailed neurological and neuropsychological assessment and written informed consent was obtained. Subsequently, we isolated DNA from blood and subjected to whole exome sequencing (WES) followed by data analysis. The variants were identified using GATK best practices pipeline and annotated using ANNOVAR. Based on online in silico prediction tools such as SIFT, Polyphen2 and CADD, the pathogenicity of the variants were determined.

Results and Discussion: We performed genetic studies on 169 patients using WES, including 154 sporadic and 15 familial EOPD cases. We identified potentially pathogenic variants in 24 patients with EOPD (14.2%) in known PD genes such as PINK1, SYNJ1, PRKN, GBA, LRRK2, MAPT. These were identified with 15 novel and 9 known variants comprising 15 autosomal dominant and 9 autosomal recessive EOPD cases.

Conclusions: Our study expands the spectrum of mutations in genes known to cause EOPD.

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Comprehensive analysis identifies lncRNA-associated competing endogenous RNA axis in the development of Squamous-subtype of Pancreatic cancer

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Pancreatic cancer is a malignant neoplasia with low overall survival rates due to its late detection, limited treatment options and its resistance to available medications. Genomic and transcriptomic analyses of pancreatic tumor have shed light on molecular heterogeneity and identified three to five molecular subtypes of pancreatic cancer. Among them, squamous subtype shows worst survival ratios even diagnosed at an early phase. However, molecular mechanism underlying the progression of squamous pancreatic tumor is not completely understood. In this regard, we made an attempt to decode the long non-coding RNAs (lncRNAs)-related competing endogenous RNA network in squamous subtype. LncRNAs, a class of non-coding RNA transcripts, play vital role in epigenetic modification and post-transcriptional regulation of target genes. LncRNAs can act as “miRNA decoys” as they bind and sequester microRNAs (miRNAs) by competing with mRNA and indirectly modulate gene expression. Dysregulation of such competing endogenous RNAs (ceRNAs) is known to be associated with pathogenesis of diseases such as cancer. Here, we studied potential regulatory ceRNA mechanism to understand pathophysiology of squamous-subtype of pancreatic cancer and to find new therapeutic targets against it. We systematically investigated the alteration in expression levels of genes, miRNAs and lncRNAs using The Cancer Genome Atlas (TCGA) data. By comparing the RNA-seq and miRNA-seq data of pancreatic cancer tissue with normal tissue, we identified 860 mRNAs, 414 lncRNAs and 52 miRNAs were differentially expressed in squamous pancreatic cancer. To gain physiologically relevant insights into the altered expression, GSEA and Gene ontology analyses were performed. Functional analysis found that the pathways viz., MTORC signalling, TGF-β signalling and processes i.e. EMT, hypoxia, protein secretion were upregulated. However, immune system-related pathways like Interleukin-6 Jak-STAT signalling, KRAS signalling, complement system, interferon-γ response and inflammatory response were downregulated. These dysregulated processes may contribute to proliferation and development of squamous tumor and tumor cells immune escape. Further, the interactions between miRNAs and mRNAs or lncRNAs were predicted using databases like miRWalk, miRDB and LncBase. An inverse correlation was observed in the expression of miRNAs and mRNAs or lncRNAs. For example, HOXA11-AS, an oncogenic lncRNA and E2F7, a transcription factor were upregulated whereas miRNA targeting these genes i.e. hsa-miR-383-5p was downregulated. This data suggest that lncRNA HOXA11-AS can increase E2F7 expression to promote cell proliferation and inhibit apoptosis of squamous pancreatic cancer by sponging hsa-miR-383-5p. Finally, we established a novel lncRNAs-miRNAs-mRNA regulatory network which will enhance our understanding of lncRNAs-associated ceRNA mechanism involved in initiation and progression of squamous subtype of pancreatic cancer. In addition to this, network topological analysis and survival analysis of each RNA in ceRNA network gave us promising prognostic biomarkers and potential therapeutic targets for squamous pancreatic cancer.

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SIGNATURE OF GUT MICROBIOME IN DIARRHEAL PATIENTS AS A PROSPECTIVE PROGNOSTIC AND DIAGNOSTIC TOOL

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Abstract

Introduction: Metagenomic analysis has evolved as a powerful tool for studying dysbiosis of microbiome associated with different diseases. It has proved to be a potential screening technique benefiting surveillance studies in epidemiology. According to the latest World Health Organization report diarrhea accounts for 525000 deaths among children under five worldwide and is the second leading cause of death among children. It affects 1.7 billion children globally, every year.

Aims and Objectives: Metagenomic sequencing of 20 diarrheal fecal samples from Kolkata was conducted to understand gut microbiome dysbiosis and to identify a microbiome signature in diarrheal patients.

Methodology: Diarrheal cohort included subjects from Kolkata and the suburban areas and included patients suffering from acute diarrhea due to different diarrheal pathogens like Eschericia coli, Vibrio cholerae, Vibrio fluvialis, Aeromonas sp., Shigella flexneri. 16S rRNA V3-V4 region was sequenced on Illumina MiSeq platform. Raw data was analysed using the MGnify pipeline and Genome Taxonomy Database (GTDB-Tk) was used for bacterial taxonomic identifcation. Simultaneously, the diarrheal pathogen in each sample was determined by culture using enrichment technique.

Results and Discussion: In all the 20 samples phylum Firmicutes, Bacteroidetes, Proteobacteria and Actinobacteria were consistently present though Firmicutes was the most abundant phylum in 11 of the samples. The Bacteroidetes/Firmicutes ratio was less than 1 in 18 samples providing a comparative index for different diarrheal pathogens. 584 genera were detected of which 18 were present in all the 20 samples revealing a core microbiota signature in the diarrheal gut. Proteobacteria was the dominant phylum in 6 samples associated with Vibrio cholerae infection. Conservation of operational taxonomic units (OTUs) was revealed among all the samples and indicated the presence of a core microbiome associated with diarrhea. In spite of patients being associated with diarrhea due to the same pathogen variable alpha-diversity indices were observed for each of them. Vibrio cholerae was identified in patients not associated with cholera and Helicobacter pylori was detected in asymptomatic patients. “Microbial dark matter” observed as signature of Candidate phyla was found. Statistical analysis revealed significant correlation of relative abundance of bacterial families of commensals and pathogens. Significant positive correlation was found between Bifidobacteriaceae and Lachnospiraceae, and Lachnospiraceae and Ruminococcaceae. Significant negative correlation was found between Ruminococcaceae and Streptococcaceae and Lachnospiraceae and Streptococcaceae. This indicated antagonistic relationship among commensals and pathobionts and symbiotic relationship among groups of commensals and groups of pathogens. These relationships in the microbial community indicate the presence of exchange communities which may be contributing to the etiology of diarrhea. These interrelations could be exploited for developing prognostic tools to prevent diarrhea in endemic population and for developing novel probiotics. The B/F ratio can be developed as a diagnostic measure of dysbiosis in diarrhea for treatment and prevention strategies.

Conclusion: This is the first comparative study of the gut microbiome associated with different diarrheal pathogens. It provided the signature of diarrheal gut microbiome dysbiosis during infection due to different pathogens. It presented the first catalogue of different bacterial taxa representing the core and variable microbiome in acute diarrheal patients.

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Genetic investigation of patients with mitochondrial membrane protein-associated neurodegeneration (MPAN)

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Objectives: To report whole exome sequencing findings in suspected mitochondrial membrane protein associated neurodegeneration (MPAN) patients.

Introduction: Mitochondrial membrane protein associated neurodegeneration (MPAN) is a subtype of neurodegeneration with brain iron accumulation (NBIA) disorder, with characteristic phenotype and radiological symptoms. The disease is caused due to mutations associated with C19orf12 gene that encodes chromosome 19 open reading frame 12. NBIA disorders are relatively rare with an incidence of 1/10,00,000 with MPAN constitutes 5 - 10% of NBIA cases and is the third most common NBIA disorder.

Methods: Whole exome sequencing (WES) was carried out using DNA isolated form the blood samples of the six suspected patients from five family. Data analysis was performed using GATK best practices workflow and variants were called. Standard filtering was carried out and potentially pathogenic variants were identified using in-silico pathogenicity prediction tool and literature curation. Subsequent segregation analysis was carried out in the family members using Sanger sequencing.

Results & Discussion: Six suspected MPAN patients from five families presenting with young onset parkinsonism with behavioral abnormality (4 patients) and spastic ataxia (2 patients, 1 family) having classical Magnetic Resonance Imaging findings of basal ganglia and substantia nigra mineralization (all patients) were included. WES followed by data analysis identified five homozygous mutations in the C19orf12 gene in six patients. We have identified three missense mutations and two novel splice-site mutations in the C19orf12 gene of the affected patients. Transcript analysis was done for one novel splice-site mutation using RT-PCR followed by Sanger sequencing. Sanger sequencing of the cDNA region of a patient with novel splice-site variant, reveals that the splice acceptor sequence for exon 3 is lost, and 22 nucleotides downstream the splice site lies the next AG sequence, which is taken as a splice acceptor site. Consequently, 24 nucleotides of the exon 3 is lost causing a loss of 8 amino acids. These 8 amino acids are part of the transmembrane region (51-71) of the protein. Unaffected mother and sister were heterozygous carrier of the variant.

Conclusion: In summary, we report two novel splice site mutations C19orf12 gene as genetic cause in a patient with MPAN. Transcript analysis of the variant affecting splice-site, establishes pathogenicity associated with the variant.

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DEREGULATION OF CIRCADIAN RHYTHM IN CHOLANGIOCARCINOMA: CircRNA PERSPECTIVE

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Circadian Rhythms (CR) are series of periodic changes regulated by spatiotemporal expression of molecular proteins. CR is instrumental in either establishment or progression of numerous pathophysiological conditions including cancers. Hence, understanding regulation of molecular clock at various levels is important. In the present study, we focused on regulation of CR in Cholangiocarcinoma (CCA) and role of circular RNAs (CircRNA) in the pathobiology of CCA. CircRNAs generated by back-splicing are known to work through their miRNA sponging ability. Therefore, circRNAs can be utilised as biomarkers and therapeutic agents in different disease conditions. In present study, we chose to explore CCA which is a rare but aggressive group of cancers originating in bile duct that largely remains incurable. We explored possible role of circRNAs in CCA condition. Towards this objective, we proceeded with curation of miRNAs capable of targeting mRNAs of selected CR clock genes from miRMap, miRDB databases and Targetscan tool. CircRNAs capable of sponging and interacting with these miRNAs were subsequently curated from CircBank database. Gene expression and miRNA expression data was taken from The Cancer Genome Atlas (TCGA) database, whereas circRNA expression data from Gene Expression Omnibus (GEO datasets). Through such data mining approach, we observed a direct correlation between CR clock gene expression and circRNA expression. Whereas we found an inverse correlation between expression of miRNAs and CR clock genes-circRNA expression. For example, CR genes, ARNTL2 and PER3, were found to get upregulated in CCA with upregulation of circRNAs hsa_circRNA_070294 and hsa_circRNA_080166 capable of sponging miRNAs hsa-miR-1295b-5p and hsa-miR-1258. These results strongly indicate a post-transcriptional alteration of CR genes expression mediated by circRNAs in CCA.

Keywords: Circadian rhythm, Cholangiocarcinoma, circRNAs, post transcriptional regulation

Genomics India 2023

CHALLENGES AND APPROACH IN UNRAVELLING OF COMPLEX SHRIMP WHOLE GENOME: POTENTIAL APPLICATION IN GENETIC IMPROVEMENT PROGRAMMES

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Aquaculture is an important contributor of seafood, provide nutritional security, and employment opportunities and constitute an economically important export commodity with high value for many countries. Aquaculture genomics identifies the candidate genes of desired and economically important traits and utilizes such information for selective breeding programs. The knowledge of the whole genome coupled with RNAseq data of shrimp would help us to establish the genes and other regulatory mechanisms controlling desirable traits in candidate species. This might potentially pave ways for devising efficient management and dietary modifications to increase growth rate and salinity adaptation of shrimps. In this study, we describe the approach, difficulties and the challenges encountered in sequencing and assembly of genomes of shrimp Penaeus indicus. The shrimp genome is complex in nature due to its high repetitive regions and large genome size. These unique features of shrimp genome are particularly challenging to decipher the whole genome assembly. The assembly of P. indicus genome was of 1.93 Gb length with scaffold N50 of 34.4 Mb and contained 28,720 protein-coding genes. A combination of PacBio, Illumina, and Arima Hi-C technologies were applied to construct the genome assembly of Penaeus indicus, an economically important brackish water aquaculture species. The genome assembly has applications in genetic improvement programs for increased productivity with desirable traits.

Keywords: Genome, Penaeus indicus, genome assembly

Genomics India 2023

CHROMATIN-TARGETING BACTERIAL HISTONE MIMIC PROTEIN AS THERAPEUTIC AGENT FOR NEURODEGENERATIVE DISEASES.

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Summary: Development of a disease-modifying therapy is the major unmet need in the management of Parkinson's Disease (PD). We report a histone-mimic, cell-permeable, hyperthermophilic bacterial protein Tm8.4 which localizes to host nuclear chromatin and imparts neuroprotective, neurodifferentiative and neuritogenic effects in dopaminergic neuronal cells. RNA sequencing analysis revealed chromatin-targeting Tm8.4 augments expression of genes involved in the transport, synthesis, and vesicular packaging of dopamine while suppressing neuroinflammatory, apoptotic and mitochondrial dysfunction related genes in 6-OHDA treated neurons. We propose that by simultaneous and directional reprogramming of signalling pathways, Tm8.4 can be developed as a translatable, disease modifying pharmacologic agent against PD.

Introduction- PD is a progressive neurodegenerative motor disorder marked by profound loss of midbrain dopaminergic neurons. Since, neuronal death and dysfunction are the major events underlying PD, therapeutic molecules which exert significant effects on neurotrophic and neuroprotective cellular mechanisms can have a huge clinical benefit. TM8.4, a histone like protein from hyperthermophilic eubacterium, has two composite nuclear localization signals. Preliminary experiments have shown that Tm8.4 imparts neuroprotection against several cytotoxic insults and exhibits neurotrophic and neuritogenic effects in dopaminergic neuronal cells.

Aim: Development of a naturally-occurring, cell-permeable, chromatin-targeting bacterial histone-like protein, Tm8.4, as a neuritogenic and neurotrophic agent in dying/dysfunctional dopaminergic neurons.

Methodology: SH-SY5Y cells and primary cortical neurons from neonatal mice were used for cell translocation and localization and biochemical and molecular analysis assays. We used morphometric analysis, qRT-PCR, Western blotting, immunocytochemistry and ELISA to demonstrate biochemical and physiological effects. We performed Next Gen sequencing based transcriptome analysis followed by qRT-PCR validation in 6-OHDA treated differentiated SHSY5Y cells.

Results: Cellular localisation studies showed that Tm8.4 accumulated in the chromatin fraction of neuronal cells in a time dependent manner. Tm8.4 treatment (1) imparted significant protection against glutamate, hypoxia and apoptosis inducing cellular insults (2) enhanced expression of neurotrophins (GDNF, BDNF), genes involved in the synthesis, storage, release of dopamine (TH, DRD2, DAT, AADC) and markers of neuronal growth and maturation (GAP43, NeuN) (3) stimulated qualitative and quantitative increase in neurite outgrowth. In primary cortical neurons Tm8.4 induced a loss of undifferentiated neuronal stem cell marker Nestin but amplified the expression of differentiated cell marker DCX and increased immunoreactivity for TH (rate limiting enzyme of dopamine synthesis) and NeuN (neuron specific nuclear protein).

Whole genome transcriptome analysis of 6-OHDA treated cells showed genes involved in transport, synthesis and vesicular packaging of dopamine (AADC, TH, GCH1, DAT), neurotrophic factors (BDNF,GDNF), survival-related proteins (phospho-Akt, CREB and GSK-3beta) were upregulated in Tm8.4 treated cells while genes involved in inflammation, apoptosis, mitochondrial dysfunction and oxidation reduction processes were downregulated.

Discussion: We have elucidated that Tm8.4 not only behaves as a natural Cell Penetrating Peptide but also imparts neuroprotection against cytotoxic agents, triggers significant neuritogenesis and induces activation of neurotrophic factors and dopamine synthesis pathway. In neurotoxin-treated cells, Tm8.4 positively targets dopaminergic signalling pathway genes while repressing inflammatory and cell-degenerative modules.

Conclusion: We have provided strong proof-of-principle evidence for Tm8.4 to be developed as a translatable pharmacologic agent against PD.

Genomics India 2023

GLUCOCORTICOID RECEPTOR DRIVEN GENES IRRESPECTIVE HORMONE RECEPTOR STATUS IDENTIFIES TUMORS ENRICHED FOR HIGHER CYTOLYTIC ACTIVITY AND LOW PROLIFERATION IN BREAST CANCERS

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Background: Breast cancer (BC) is the most frequently diagnosed cancer worldwide and second most common cancer among women in India. The glucocorticoid receptor (GR) is an important marker in BC and GR activation has been reported to be different between breast cancer subtypes. Activation of GR in ER-negative human breast cancer cell lines has been shown to promote cancer cell survival, chemotherapy resistance, and increased tumor growth. Reports suggest that high GR expression is correlated with a poor and good prognosis in ER- and ER+ BCs, respectively. It is addressed that this difference is due to an interaction of the GR and ER. We hypothesize that there is a difference between GR-high and GR-low tumors regardless of ER status.

Method: We developed a bioinformatic pipeline using an integrated method by incorporating protein interaction networks, topological parameters, and semantic similarity to derive GR driven genes using publicly available microarray data sets obtained from GR positive BC cell lines treated with Dexamethasone (Dex). Gene set enrichment analysis was performed using r package fgsea. Genes identified through the pipeline were classified into three groups based on the context of expression of Estrogen Receptor (ER) as GR regulated genes in absence of ER, in presence of ER and irrespective of ER. Gene score was derived using the mean expression GR regulated genes irrespective of ER status and distribution of the score was examined in the METABRIC cohort. Tumors were divided into GR low and GR high groups based on the median gene score cut off and survival between the groups was compared by Kaplan Meier analysis. Further, association of gene score with immune cell distribution, tumor cell proliferation (MKi67, PCNA and MCM6), epithelial to mesenchymal transition (77 gene signatures) and stemness (CD44, ALDH1A1 and PROM1) was compared between the groups.

Results: We identified 21 genes driven by GR irrespective of ER status and 15 genes with similar trend of regulation. The pathway enrichment analysis has shown upregulation of pathways like Androgen response, Estrogen response early and late, Glucocorticoid receptor pathway, Adipogenesis, Hypoxia and Nuclear receptors meta-pathway. The key genes that contributed to Glucocorticoid receptor pathway were LRRC8A, B3GNT5, RGS2 and ANGPTL4. Tumors with high gene score were associated with longer overall and relapse free survival ($p<0.0023$ and $p=0.047$ respectively) and had significantly low proliferation ($p=1.8\times10\text{-}11$) and higher cytolytic activity ($p<2\times10\text{-}16$). However, we observed increased EMT and stemness markers in tumors with high gene score (for both $p<2\times10\text{-}16$). In addition, we observed higher proportion of anti-tumorigenic cell types like M1 macrophages (0.0232), CD8 Tcells (0.00013), Bcells (1x10-07) and Natural Killer cells (0.02716).

Conclusion: Our results indicate GR high breast cancers are likely to be etiologically and biologically different from GR low breast cancers. Findings of our study need to be explored in more datasets and association of gene score with EMT and stemness needs validation by in-vitro studies.

Genomics India 2023

Study of Odisha tribal gut microbiome in comparison with rural non tribal and urban population

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Abstract:

The significance of gut microbiome research to understand human health and well-being is getting widely recognized. Several studies have revealed the importance of gut microbiome in maintaining homeostasis and loss of which may result in a diseased state. Moreover, the role of secondary metabolites released by gut microbes is gaining scientific importance due to its role in regulating several biological processes in humans. The composition and diversity of gut microbiome is dependent on several variables such as location, environment, lifestyle, food, ethnicity, etc. The studies on gut microbiota in different ethnic groups can provide valuable information on microbial biodiversity, which can help us to identify microbes having probiotic or other therapeutic potential. Scanty work progress has been made on this area of research. In this study, we have attempted to understand microbial diversity and functional characteristics of the gut microbes present in the tribal communities of Odisha, India. Towards this, we have investigated the gut microbiome of eight ethnic tribes from three tribal dominated districts of Odisha. We have conducted studies on 258 individuals gut microbiota belonging to Munda, Oraon, Paroja, Bhatra, Gond, Santal, Bhuyain and Juang tribes located in Sudergarh, Nabrangpur and Keonjhar districts and compared with 43 non-tribal (rural) and 41 urban gut microbiome. DNA was extracted from the fecal samples and subjected to 16S rRNA gene (V1-V9 regions) sequencing using the Oxford Nanopore platform. We found that the gut microbiome of the tribal communities were dominated by the Firmicutes, Bacteroidetes, Proteobacteria, and Spirochaetes. There were 23 core bacterial genera and 24 core bacterial species that were identified across the three different communities, however we observed that the overall gut bacterial composition exhibited unique patterns and was affected by the topographical region. Comparing blood biochemistry profiles revealed significant correlation of gut microbiome with abnormal HDL and LDL profiles, which was associated with opportunistic pathogens like *Prevotella intermedia, Prevotella denticola*, and *Prevotella jejuni*.

Genomics India 2023

IN-SILICO IDENTIFICATION AND ANALYSIS OF MITOCHONDRIAL RNA EDITING EVENTS IN HELIANTHUS SPECIES

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Abstract : RNA editing is an important post-transcriptional modification that leads to genomic and proteomic diversity. The advent of RNA-Seq has facilitated fast and accurate sequencing of transcriptomes to study the editing effects. We discovered 687 editing events for the first time using computational methods and characterised them based on genotype, specie and stress specific RNA editing events.

Introduction: RNA sequence alteration occurs due to RNA editing which is a post transcriptional modification. It causes a deviation from the genomic DNA sequence resulting in RNA-DNA differences. Sunflower is one of the most used commercial oilseed crops. The number of editing sites varies greatly among land plants and between the organellar genomes. Accurate study of RNA editing events in diverse species is possible by NGS based methods.

Aim: To catalogue all RNA editing events in the transcriptomes of Helianthus species.

Objectives:

- Transcriptome sequencing of four species of Helianthus (Helianthus annuus, H. debilis, H. praecox and H. niveus) and three genotypes of H. annuus (2023B, TX16R and ID25) and respective pathogen infected variants.
- Reference-based alignment of the sequenced reads onto H. annuus genome.
- Identification of RNA editing events.
- Analysis and comparison of editing events at genotype, specie specific and stress specific levels.

Methodology: The plants of the species were grown and infested. Library preparation was performed based on Illumina TruSeq RNA library protocol by Illumina Technologies (San Diego, CA). The reads were aligned on to the indexed reference mitochondrial genome using bowtie2 We used a pipeline comprising REDItools (Version1.2) to obtain RNA editing events from transcriptome data. In-silico validation of the RNA editing sites was performed using SNPEff and comparative analysis was done manually.

Results: We discovered 687 editing sites, 220 editing events in the protein-coding regions, among all species and genotypes considered in this study. These included “C toU” and “U to C” RNA editing events. On further analysis, we observed that these editing events include 14 different types of amino acid changes that involve a creation of two stop codon events. The conserved editing sites identified were 247 accounting to ~36% of all the editing sites identified. In this study, we observed 85 edit sites that are specific to pathogenic stress infected variants and these could be called as stress-specific edit sites. It was noted that the highest number of edit sites were observed in H. niveus sample (31).

Discussion and Conclusion: This study provides a detailed picture of the Helianthus species mitochondrial RNA editing status. We have identified and characterized genotype, species-specific RNA editing events for the first time and stress-specific RNA editing events which may be useful as a potential source for evolutionary, development and stress responsive studies in future.

Genomics India 2023

Single nucleotide polymorphisms predisposes risk factors for cardiovascular diseases in Indians

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Summary:
WHO data in 2016 reported 27% total deaths in India were attributed to Cardiovascular diseases (CVDs). Despite a high disease burden, awareness and steps for risk reduction are fairly poor. Incorporation of genetics into risk prediction by Polygenic risk scores (PRS) can help improve outcomes of risk reduction.

Introduction: Cardiovascular disease (CVD) presents itself a decade earlier in the Indian population as compared to others. Premature mortality in India due to CVD has increased by 59%. Hypertension, diabetes and cholesterol, among others, are considered major risk factors. The prevalence of hypertension in adult Indians is estimated to be 34% in urban and 28% in rural areas. Prevalence of diabetes mellitus has almost doubled in the past 20 years, from 9% to 17% in urban areas and quadrupled from 2% to 9% in rural areas. In addition, increasing stress, higher fat proportion and limited physical exercise are contributing factors.

Aim: To understand the presence of genetic risk factors for CVD in individuals with and without personal history of CVD or risk factors associated with CVD.

Methodology: We stratified a small representative set of patients who have taken up direct to consumer testing for identifying genetic predisposition due to SNPs related to cardiovascular diseases and their risk factors. Post test genetic counseling was offered to understand the impact of genetic and non-genetic risk factors (lifestyle, diet, family history) and provide a personalized actionable plan for risk reduction and management. The genetic risk factors associated with cholesterol, hypertension, diabetes mellitus and triglycerides were included.

Results: Our representative sample size was 44. 22 (M=15 F=7) patients with personal history and 22 (M=12, F=10) patients without personal history of CVD or associated risk factors. 18 patients had 2 out of 4 scores conferring a high genetic risk. 12 of these had a personal history of a disease and 7 of these were males. Further, 9 patients had 3 out of 4 risk scores. 4 of these had a personal history of disease and 2 of these were males.

Discussion: We saw a higher prevalence of genetic risk factors in males and in individuals with a personal history of disease. The average age of individuals with risk factor but no personal history of disease is about 7-8 years younger. Early identification of the predisposition, rigorous screening and healthy changes in diet and lifestyle can help reduce the occurrence of disease. Identification of SNPs can also help to optimize drug therapy and reduce toxicity of medications to manage CVD.

Conclusion: The American Heart Association has suggested stratifying risk by PRS to identify high-risk subgroups for whom successful lifestyle modification may be recommended to reduce risk for CVDs.

Genomics India 2023

SARS-COV-2 VARIANT RACE IN MUMBAI: A CHRONOLOGY

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Introduction:
Genome Sequencing facilitated rapid identification of variants of SARS-CoV-2, development of diagnostic tools and investigating the global dissemination. The staggering impact of the RNA virus can be attributed to the high mutation rates facilitating the adaptation to the host. Therefore, continued genomic surveillance complements, augments and support appropriate public health management to reduce the burden of COVID-19.

Aim and Objectives: To time-track the trend of SARS-CoV-2 variants in Mumbai

Methodology:
Genome Sequencing Centre for Outbreak Preparedness & Epidemiology (GeSCOPE) is a public health Genome sequencing Lab in Brihanmumbai Municipal Corporation receiving positive samples from public & private Labs across Mumbai. This study was conducted on 4756 SARS-CoV-2 samples collected between March 2021 and October 2022. Samples were processed using the COVIDSeq protocol, which involves cDNA synthesis, amplification, and barcoding of the libraries. The sequencing of samples was done on NextSeq™ 2000 system (Illumina Inc., USA) using P2 (100 cycles) v3 kit for high-throughput detection and deciphering the genetic epidemiology of SARS-CoV-2. The raw data was processed using DRAGEN COVIDSeq Test Pipeline v1.0.20 (Illumina Inc.) that involves Sample Sheet validation, Data Quality Checks, FastQ generation and detection of SARS-CoV-2 on the Illumina DRAGEN v3 BioIT platform. The SARS-CoV-2 genomes were assigned lineages using Phylogenetic Assignment of Named Global Outbreak LINeages (PangoLIN, v4.1.3) software suite.

Results:
We detected 148 lineages of SARS-CoV-2 circulating in Mumbai in a span of 20 months. The second COVID-19 peak in Mumbai was driven by Delta variant (B.1.617.2) and its sub-lineages primarily AY.112, AY.120 and AY.127. Also, observed in March and April was B.1.617 strain with characteristic E484Q and L452R mutations. The study captured the transition of Omicron from 2 cases with travel history in November 2021 to its 100% prevalence. While BA.1.*, was the predominant strain observed in the initial phase (December 2021-Early January 2022) of the Omicron wave, it was swiftly replaced by BA.2 by February 2022 and closely followed by its sub-lineages mainly BA.2.10 and BA.2.38. There was a decline in the proportion of BA.2 starting in March to be completely substituted by its descendants BA.74, BA.75 and BA.2.76 in June 2022 and finally to sub-lineages of BA.2.75, BA.2.10, BA.5 and their recombinants (XBB.*)

Discussion and Conclusion:
The study provides a consolidated perspective on the proportion and peaks of the variants circulating in Mumbai over 20 months which has been useful in determining the impact of the strains on the clinical outcomes and spread within the population. Continued monitoring of circulating strains is of utmost importance to swiftly detect a novel lineage and/or mutations of potential clinical importance. In a densely populated city of Mumbai that has an added burden of co-morbidities, even milder variants could have a huge impact. Continuous Genomic surveillance empowers us with the information required to design and implement appropriate measures to prevent & control the spread of infection.

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