CHAPTER 57

ZOOLOGY

Doctoral Theses

01. BEHERA (Manisha)

Expression of Bacteriophage Endolysin for Mitigation of Methicillin-Resistant Staphylococcus aureus Infection.

Supervisor: Prof. Soma Mondal Ghorai

Th 28520

Abstract

The overuse and misuse of antibiotics in the treatment, and control of bacterial infections has led to the development of different antibiotic-resistant strains of Staphylococcus aureus. The continuous evolution of antibiotic-resistant methicillin-resistant Staphylococcus aureus (MRSA) is a major cause of mortality and morbidity in hospitals, communities, and livestock sectors. This lays out the need to develop novel antimicrobials with higher activity and lower resistance against MRSA. This study includes the expression of novel chimeric bacteriophage endolysin CHAPk-SH3bk derived from endolysin LysK to investigate its antibacterial activity against planktonic and biofilm-forming MRSA. The bactericidal and anti-biofilm activity of CHAPk-SH3bk was also compared to chimeric construct CHAPk. The molecular docking and MD simulation results identified critical amino acids (ASP47, ASP56, ARG71, and Gly74) of CHAPk domain responsible for its catalytic activity. Chimeric endolysin CHAPk-SH3bk showed an effective binding to peptidoglycan fragment forming 14 hydrogen bonds. The in-vitro antibacterial assays displayed higher activity of 0.2µg/µl CHAPk against planktonic MRSA with 2-log10 reduction in 2 hours. The 0.02µg/µl of both CHAPk and CHAPk-SH3bk displayed bactericidal activity against MRSA with ~4log10 and ~3.5log10 reduction post 24 hours of treatment. The 0.05µg/µl of CHAPk-SH3bk reduced biofilm more effectively from plastic, glass, and steel surfaces of hospital-associated MRSA S. aureus (ATCC® BAA-44™) and bovine origin MRSA isolates. The biofilm reduction was further confirmed using live/dead DAPI/PI staining confocal laser scanning microscopy and scanning electron microscopy. The 0.05µg/µl of CHAPk-SH3bk was more effective in inhibiting biofilm formation of hospital-associated MRSA and CHAPk was effective against bovine-origin MRSA strains. The biofilm inhibition was further confirmed using live/dead DAPI/PI staining confocal laser scanning microscopy. The 0.5µg/µl of CHAPk-SH3bk and CHAPk displayed 100% cell viability against MDCK cell lines. The 0.5µg/µl of CHAPk-SH3bk displayed higher biofilm reduction ability compared to 0.5µg/µl of CHAPk on 24-hour biofilm in mice skin infection model. The ex-vivo histological studies (H&E, Gram staining, and Immunohistochemistry) displayed an effective lytic activity of 0.05µg/µl CHAPk-SH3bk against MRSA S. aureus (ATCC® BAA-44™), that was further confirmed by CLSM and SEM analysis. This study indicates an effective reduction of preformed MRSA biofilms using novel chimeric construct CHAPk-SH3bk in in-vitro, and in-vivo skin-infection model. The ex-vivo histology study confirms the in-vitro and in-vivo study results. Thus, this corroborates that the combination and shuffling of different domains of phage endolysin potentially increase its bacteriolytic effectiveness against MRSA.

Contents

1. Review of literature 2. Design, In-silico Analysis, Molecular Cloning, Expression, and Purification of Novel Chimeric Endolysins 3. Isolation of Antibiotic-Resistant E. coli and S. aureus from Mastitis-Infected Milk Samples 4. In-vitro Anti-staphylococcal activity, Biochemical Characterization, and Anti-biofilm Activity Analysis of Chimeric Endolysins 5. In-vivo and Ex-vivo Anti-staphylococcal and Antibiofilm Activity Analysis of Chimeric Endolysins. Summary. List of Publications and Poster Presentations.

02. HIMANSHI

Assessing the Health Risks of Radiofrequency Radiations: A Multi-Level Approach.

Supervisors: Prof. Rita Singh and Dr. Rajeev Singh

Th 28820

Abstract

Given the rapid growth of communication technology, research on cellphone radiation is increasingly vital. This study uses a multi-level approach, combining a cross-sectional analysis of its correlation with health indicators and an in vitro investigation of cellular effects. For the cross-sectional study, students, potentially more sensitive to RFR exposure due to ongoing development, were selected. Data on cellphone use, sleep patterns, insomnia, psychological well-being, migraines, and demographics were gathered via an offline questionnaire. For the cellular study, monocytes, chosen for their sensitivity to environmental stressors and their limited known response to RFR, were exposed to 2318 MHz radiation for 15-120 minutes at 0.224 W/m^2, followed by immunological assays. Questionnaire analysis showed that longer cellphone usage was significantly associated with greater psychological distress ($F = 9.211$, $P < 0.001$) and insomnia ($F = 6.958$, $P < 0.001$), and reduced sleep quality ($F=9.841$, $P < 0.001$). Overall, the findings indicate that prolonged usage negatively impacts sleep, increases insomnia risk, and heightens stress and headache incidence in students. The cellular study showed time-dependent effects of RFR exposure. A 30-minute exposure markedly increased pro-inflammatory cytokine levels, reactive species generation, and JNK and p38 MAPK activity, with no change in ERK activity. In addition, RFR induces ROS mainly from cytosolic sources, with NADPH oxidase as the primary contributor, rather than mitochondria. At 60 minutes, RFR significantly reduced monocyte phagocytic activity. Interestingly, the irradiated cells regained normal function until the final 120 minutes of exposure. However, prolonged exposure (120 minutes) led to the inhibition of ERK, JNK, and p38 MAPK activity, while also inducing significant DNA damage. In contrast, early RFR exposures suppressed NF-κB p65 activity with increased IκB-α stabilization, suggesting a temporary inhibition of NF-κB signaling. Overall, these findings indicate short-term adaptation but long-term cellular dysfunction and genomic instability, highlighting the need to limit cellphone use.

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1. Introduction 2. Questionnaire-based health survey of university students using cell phone 3. Time-dependent effect of radiofrequency radiations on human leukemia monocyte cell functions 4. Time-dependent effect of RFR on key signaling proteins and DNA integrity in monocytes, with identification of the primary RFR-induced ROS source. Summary. References. List of publications and posters presented.

03. JAIN (Kusum)
Molecular Mechanism of Azole Antifungal Resistance in Non-Albicans Candida Species and Exploration of New Derivatives, as Potent Antifungal.
Supervisor: Prof. Hardeep Kaur
Th 28521

Abstract

Fungal infections caused by Candida species, represent a significant global health burden, especially in immunocompromised individuals. In last decade, non-albicans Candida (NAC) species, have emerged as prominent pathogens, often demonstrating multidrug resistance, complicating treatment options. This study focuses on identifying NAC species by using MALDI-TOF MS, and ITS sequencing. Further their antifungal susceptibility profiles (AFST) were evaluated by using the broth micro-dilution method as recommended by CLSI. Among 500 NAC isolates, six species, including C. tropicalis (n=170), P. kudriavzevii (n=165), N. glabrata (n=70), C. parapsilosis (n=52) and C. auris (n=30), L. elongisporus (n=13) were identified. AFST revealed varying azole resistance patterns, with 17.6% of C. tropicalis isolates resistant to fluconazole and 30% cross-resistant to voriconazole. P. kudriavzevii showed 87.3% of isolates exhibiting high fluconazole MIC values (16-32 mg/L). Meanwhile, C. auris displayed high resistance to fluconazole (90%) and low susceptibility to voriconazole (30%). Genetic analysis, including target gene sequencing, whole-genome sequencing, RT-PCR and transcriptomic profiling, was employed to investigate azole resistance mechanisms in P. kudriavzevii and C. tropicalis. Molecular analyses of azole resistance mechanisms in C. tropicalis identified key point mutation i.e A395T and C461T and overexpression in azole target ERG11 gene. Whereas in P. kudriavzevii, overexpression of ABC transporter gene is important for reduced azole susceptibility. However, fluconazole susceptibility in P. kudriavzevii seems to be more complex and regulated by other than ergosterol biosynthesis pathway. Furthermore, the study explored the antifungal potential of biosynthesized silver nanoparticles from marine diatoms, demonstrating significant activity against resistant strains of C. auris and P. kudriavzevii. Understanding the molecular basis of antifungal resistance in NAC species is crucial for developing targeted therapies and managing the increasing threat posed by these pathogens. The findings underscore the importance of accurate species identification, understanding resistance mechanisms, and the development of novel antifungal therapies to combat NAC species.

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04. MAURYA (Swati)
Spatial-Temporal Variability in Abiotic Factors and their Impact on Ciliate Community Structure in Terrestrial Ecosystems.
Supervisors: Prof. Ravi Toteja and Prof. Seema Makhija
Th 28771

Abstract

Ciliates play a vital role in the terrestrial microbial loop by improving soil quality through nutrient recycling. These microorganisms graze on bacteria, algae, and fungi, releasing secondary nutrients that influence microbial community structures. Soil health, however, is deeply impacted by human activities such as urbanization and land-use changes, leading to erosion and ecological imbalance. As a result, ciliates have emerged as powerful bioindicators due to their diversity, rapid community shifts, and environmental sensitivity. Various soil parameters, including Water Holding Capacity (WHC), pH, Electrical Conductivity (EC), Soil Organic Matter (SOM), Calcium Carbonate (CaCO3), Calcium and Magnesium (Ca2+ & Mg2+), Nitrogen (N), Cation Exchange Capacity (CEC), and heavy metal concentrations, were analyzed across three sites: Jahanpanah City Forest (J), Okhla Landfill (L), and Okhla Sewage Treatment Plant (S). Significant spatial and temporal variations were observed among different sites. Site J proved most favorable for ciliate growth, with spring and autumn being peak seasons for diversity. Microscopic analysis identified predominant classes such as Spirotrichea, Colpodea, and Litostomatea, alongside additional classes like Nassophorea, Heterotrichea and Prostomatea using eDNA metabarcoding. Spirotrichea, Colpodea and Oligohymenophorea were found to be the most predominant classes in both morphological and molecular approaches. Notably, three new Colpoda species—Colpoda minima n. sp., Colpoda indica n. sp., and Colpoda amicronucleata n. sp.—were discovered. A draft genome sequencing of Colpoda minima n. sp. revealed a GC content of 60% and over 5,502 annotated genes. Presence of multiple copies of genes related to antioxidant mechanisms and apoptosis bolster survival in adverse conditions. These findings highlight ciliates` significance in environmental monitoring, biodiversity conservation, and genomic studies. The research underscores their role as ecological bioindicators, offering valuable insights into soil ecosystem quality and advancing scientific understanding.

Contents

05. PRIYANKA

Characterization of Asprosin in Spotted Snakehead Channa Punctata and its Possible Role in Reproduction.

Supervisors: Prof. Brototi Roy and Prof. Umesh Rai

Th 28523

Abstract

Asprosin is a glucogenic protein hormone, encoded by the C-terminal region of FBN1 gene. FBN1 encodes a 2871 amino acid pre-profibrillin protein, which is cleaved by furin enzyme near the C-terminal, resulting into fibrillin-1 and asprosin. Many studies have shown its important and diverse physiological role in mammals. Despite its importance in mammalian physiology, till date, there are no studies of this hormone in non-mammalian vertebrates. In light of this, current study has been carried out to explore asprosin and its function in teleosts Channa punctata. The transcript of spotted snakehead Channa punctata fbn1 gene has been retrieved,

which encodes 2817 amino acid putative profibrillin protein. The presence of conserved furin cleavage site was observed near the C-terminal of profibrillin in C. punctata. Further, differential expression of fbn1 was observed in various tissues with highest expression in the gonads of C. punctata. Also, prominent expression of furin was observed in the gonads. Using in silico analysis, the physicochemical properties and post-translational modifications of putative spotted snakehead asprosin were predicted and tertiary model was constructed. The recombinant asprosin of C. punctata has been purified and used for further in vitro studies. The fbn1 showed a reproductive phase-dependent expression in testis and ovary of C. punctata. Asprosin significantly enhanced the expression of gonadotropin receptor, sex steroid receptor, gametogenic and steroidogenic marker genes in testis and ovary of C. punctata upon treatment with recombinant asprosin. High cAMP levels were measured in testicular pieces upon asprosin treatment indicating involvement of GPCR-cAMP pathway in testis. Another receptor of asprosin, ptprd was characterized and molecular docking of asprosin with the ligand-binding domain of ptprd was performed to identify the key residues involved in interaction. The energy minimization using MD simulation of docked structure showed the stability of asprosin-ptprd complex.

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06. PRIYANKA

Studies on Bioefficacy and Mode of Action of Cassia fistula Leaf Extract on Red Cotton Bug, Dysdercus koenigii Fabricius (Hemiptera:Pyrrhocoridae).

Supervisors: Prof. Kamal Kumar Gupta and Prof. Rajendra Kumar Pandey

Th 28524

Abstract

Dysdercus koenigii Fabricius (Heteroptera: Pyrrhocoridae) is a serious pest of cotton and other plants of family Malvaceae. The control of this pest using chemical insecticides has detrimental effects on the environment and human health. Therefore, present study aimed at investigating environment friendly and sustainable methods for the pest control. Insecticidal, growth regulatory and development-suppressive bioefficacy of Cassia fistula acetone leaf extract (Cf-ALE) prepared from the leaves collected during spring and autumn were studied against fifth instar nymphs of D. koenigii. Cf-ALE showed seasonal variations in their nymphicidal activity; it was more prominent in Cf-ALE (spring) with median lethal dose (LD50) 17.7 µg/insect and inhibition of adult emergence (IE50) 12.02 µg/insect. Development anomalies and a significant decrease in the growth index were also observed as a result of treatment. LC-MS results showed season specific differences in the phytocompounds in the extracts, with more insecticidal compounds such as catechins, quercetin, rutin in spring season extract. Treatment of fifth instar nymph with Cf-ALE resulted in a decrease in the total haemocyte count (THC). Results of differential haemocyte count showed significant difference in the number of prohaemocytes, plasmatocytes, adipohaemocytes, granulocyte, oenocytoid and disintegrated cells in the treated nymphs. Scanning electron microscopy showed deformity in surface morphology, ruptured plasma membrane and fat droplets in the

oenocytoids and adipohaemocytes. Fluorescence-Activated Cell Sorting (FACS) flow cytometry showed significant increase in the number of dead haemocytes. The Cf-ALE at LD50 caused significant change in the protein profile of haemolymph and midgut. Docking interactions of quercetin and rhein with selected proteins reflected highest binding affinity of peroxidase with quercetin and heat shock protein cognate 70 with rhein. It was inferred that the Cf-ALE may cause oxidative damage by affecting detoxifying and antioxidant enzymes, and impaired immunological responses by altering protein profile and haemocyte count of the treated nymphs.

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07. SANKAR (Manu)
Studies on the Synergistic Efficacy of Verapamil on the Growth Regulatory Impact of Diflubenzuron on Aedes aegypti L. (Diptera: Culicidae).
Supervisor: Prof. Sarita Kumar
Th 28522

Abstract

Aedes aegypti is a vector of several arboviral diseases of human concern. The control of vector relies on the use of traditional synthetic insecticides which has caused development of resistance in mosquitoes and lethal effects on environment. This has demanded the need of eco-safe and target-specific insect growth regulators (IGRs). This study compared the growth regulatory effects of Diflubenzuron (DFB), an IGR, on lab-reared (AND-Ae. aegypti) and wild-caught (GVD-Ae. aegypti) strains of Aedes aegypti. The study revealed the efficacy of DFB causing dose-dependent adult emergence inhibition and ovicidal effects in Ae. aegypti. The use of DFB-verapamil (DFB-V) enhanced the impact indicating the synergistic effects. Furthermore, treatment with IE30 and IE50 dosages of DFB/DFB-V demonstrated compromised physiological and reproductive fitness in both the strains inhibiting growth and adult emergence, and lowering oviposition and egg hatch. The negligible toxicity of IE50 DFB/DFB-V to non-target organisms indicated their suitability for field use. DFB and DFB-V treatments induced varying effects on detoxifying enzyme levels reducing α-esterase and Glutathione S-transferases while increasing β-esterase, acetylcholinesterase, and CYP450-monooxygenases showing their role in immunity. Similarly, DFB and DFB-V treatment resulted in varied activities of antioxidant enzymes, Superoxide dismutase, Catalase, and Glutathione peroxidase in larvae. In addition, DFB treatment decreased chitin content in both the strains, higher reduction recorded with DFB-V. On the other hand, DFB increased and DFB-V decreased cuticular thickness. The wild-caught larvae had greater thickness indicating cuticular penetration as a defense mechanism. Finally, AND-Ae. aegypti larvae showed upregulated ABCB4 (>7-fold) and ABCB6, and downregulated ABCG4 gene expression. In contrast, DFB reduced ABCB2, ABCB4, ABCG4, and ABCB6 gene expression in GVD-Ae. aegypti, while DFB-V upregulated all genes, suggesting the effects of verapamil, an ABC transporter inhibitor. The study provides valuable

insights into the potential use of verapamil as an efficient synergist of DFB in mosquito management programs.

Contents

1. Review of literature 2. Materials and Methodology 3. Efficacy of DFB and DFB-V on survival, growth, development, and reproductive fitness of Aedes aegypti 4. Impact of DFB and DFB-V on the metabolic detoxification and growth-related antioxidant enzyme activities in Aedes aegypti 5. Effects of DFB and DFB-V on the larval cuticular thickness and chitin content of eggs and larvae of Aedes aegypti 6. Effects of DFB and DFB-V on the expression of ABCB2, ABCB4, ABCG4 and ABCB6 genes in larvae of Aedes aegypti 7. Discussion 8. Summary and Conclusion. References and List of Publications.

08. SHARMA (Nitika)
Assessment of Soil Health in the Pranmati Basin, Chamoli, Uttarakhand: Physico-chemical Parameters, Enzymatic Activity and Bacterial Diversity.
Supervisor: Prof. Neeta Sehgal
Th 28525

Abstract

The present study discusses bacterial communities importance in soil health and ecological balance across various landforms, including forest land, flood zone land, agricultural fields, and polluted sites. The research assesses soil health through physico-chemical parameters, enzymatic activities, and bacterial diversity. Findings indicate that acid phosphatase activity is notably high in soils from the Pranmati basin, characterized by sandy, non-saline soil and slightly acidic to neutral pH levels. Metagenomic analysis reveals an extensive diversity of bacteria, cataloguing 49 phyla, 156 classes, 367 orders, 626 families, and 1465 genera. Notably, six bacterial strains have been isolated from the Pranmati basin`s diverse landforms, providing further insight into local microbial communities. Elevation and community structure study which has been undertaken in two sub-catchments (Ratgaon and Ruisan) and the mouth of the Pranmati basin, shows that bacterial communities vary with altitude, influenced predominantly by abiotic factors and climatic conditions. Altitudinal shifts in bacterial diversity have showcased 39 phyla, 119 classes, 280 orders, 448 families, and 907 genera. Phylogenetic analysis using 16S rRNA sequences highlights metabolic functions essential for microbial survival, especially in nutrient-deficient and competitive environments. These findings suggest that soil health is stable and fertile in undisturbed forest lands and moderately disturbed agricultural lands, whereas severely impacted sites, such as flood zones and polluted lands, exhibit poor soil health. In summary, the study enhances the understanding of soil health and the role of native bacteria in different environments, which is crucial for effective environmental management and ecosystem restoration in the Pranmati Basin of the Himalayas, Uttarakhand. By elucidating the interactions and functional adaptations of these microbial communities, the research contributes valuable insights into maintaining soil health and ecosystem functioning in critical zones.

Contents

1. Review of literature 2. Introduction 3. Material and Methods 4. Results 5. Discussion. Summary. References and List of Publications.

09. SINGH (Priyanka)

Magneto-nanotherapy Targeting Ferroptosis in Rheumatoid Arthritis: Mangiferin Loaded Chitosan Coated magnetite nanoparticles with Folic acid (MGF- ChMNPsFA) mediated redox rewiring and macrophage reprogramming to alleviate inflammation both in-vitro and in-vivo.

Supervisor: Prof. Anita Kamra Verma

Th 28526

Abstract

Rheumatoid arthritis (RA), an autoimmune disorder resulting in joint inflammation causing damage to cartilage, bones, and ligaments with impaired mobility. Literature survey indicated ferroptosis in initiation and progression of RA. Ferroptosis is a regulated cell death characterized by iron-dependent lipid peroxidation and oxidative stress, leading to depletion of glutathione in RA. MGF loaded Chitosan coated magnetite nanoparticles with Folic acid (MGF-ChMNPsFA) were fabricated by chemical synthesis and characterized using DLS, FESEM, XRD, FTIR, VSM in presence of SMF 0.2T. IC50 of MGF, ChMNPsFA, MGF-ChMNPsFA were calculated post-LPS stimulation of RAW264.7 cells and peritoneal macrophages. Cellular uptake of FITC-ChMNPsFA indicated internalization. In presence of SMF 0.2T, decreased ROS and oxidative stress post-treatment with MGF-ChMNPs-FA was observed. Down-modulation of TNFα, NFkB activity and enhanced antioxidant NRF2 expression levels indicated macrophage reprograming confirmed by expression of polarization markers M1(iNOS) and M2 (ARG1). High lipid peroxidation confirmed ferroptosis in M1-macrophages. Biocompatibility was assured by negligible hemotoxicity. Improved pharmacokinetics and accumulation of MGF-ChMNPsFA in RA joints was observed when compared to MGF per se. Anti-arthritic activity of MGF-ChMNPsFA was validated by photography, X-ray, Micro-CT analysis of the ankle joint, and histopathology. Decreased TNF-α and IL-6 with enhanced IL-10 and TGF-β levels along with immunohistochemistry confirmed macrophage reprograming assessed by specific protein markers (CD68/CD163/ARG1/ STAT6). MGF-ChMNPsFA modulated apoptosis following polarisation signalling pathway (NRF2 and JNK/STAT6) for downmodulation of inflammation. MGF exerts its anti-RA effects partially through inhibition of macrophage ferroptosis, acting as a direct inhibitor of Keap1 promoting Nrf2 activation. Inhibition of ferroptosis by MGF rescues M2 macrophages and alleviates arthritis by suppressing the NRF2-ROS nexus and NFkB in M1 macrophages. Hence, MGF-ChMNPsFA might be a promising anti-ferroptotic agent when used along with static magnetic field. This work can address the research gap in clinics where magnetic therapies for RA are used.

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10. VERMA (Kavita)
Effect of Phenanthrene and Fluoranthene on Insect-Plant-Microbial Interactions.
Supervisor: Prof. Vartika Mathur
Th 28527

Abstract

In agroecosystem, Polycyclic aromatic hydrocarbons (PAH) are considered as persistent organic pollutants and their chemical stability and hydrophobic nature pose significant threat to soil health, crop productivity and environmental sustainability. Phenanthrene (PHE) and Fluoranthene (FLU) are among the most abundant low and high molecular weight PAH, respectively, found in environment. Despite their widespread occurrence, there are limited studies on the effects of these priority pollutants on insect-plant-microbial interactions and their bio-accumulation from rhizosphere to plant and further to insect. My study has demonstrated that 75, 100 and 200 mg/kg of PAH supplementation in rhizosphere soil caused a significant shift in the soil microbiome composition. There was significant reduction in nutrient profile of soil and microbial enzymatic activity as well as increase in colony forming units of rhizosphere microbes under stress condition. Moreover, tomato plants growing in this soil accumulated significant amount of PAH, leading to induced stress response in them. PAH accumulation in tomato resulted in delayed phenology, reduced growth, increased microbial density and altered primary (chlorophylls, carotenoids, total sugar and total soluble protein) as well as secondary responses (phenol, condensed tannins and antioxidants). In both terrestrial and terrestrial ecosystems, insects form the foremost part of biodiversity, and are known as the drivers of major ecological services. In my study, increased endosymbionts density, morphological diversity, larval weight, peroxidase, catalase and SOD activity and mortality rate have been observed under both Phe and Flu stress. However, there was a reduced feeding preference of Phe and Flu contaminated leaves. Higher transfer of both Phe and Flu took place at 100 mg/kg of concentration in plants from rhizosphere. This study for the first time explores the effect of these PAH on insect-plant- microbial interactions, providing not only novel insights into ecological impacts of these pollutants, but also their effect on the agroecosystem.

Contents

11. YADAV (Anamika)
Exploration of Environmental Niches for Candida Auris and its Resistance Mechanisms Against fluconazole.
Supervisors: Prof. Hardeep Kaur and Prof. Anuradha
Th 28528

Abstract

My work is about the exploration of environmental niches for Candida auris, for this different fruit species, soil samples from different sites, and dogs were explored. In this study C. auris were isolated from the surface of apples and dogs. It was hypothesized from this study that there should be a common environmental source for the colonisation of these apples and dogs and then these are transferring the same C. auris to other sources like other animals and humans as well.

Metabarcoding analysis confirmed the culture results. For the isolated C. auris different morphological characterization, susceptibility profiling and whole genome sequencing (WGS) was done to check if these strains are different from clinical strains or carrying the same genotype as of clinical strains. By the results of these analysis, we come to know that these isolated C. auris strains are sharing the same susceptibility pattern as of clinical strains, found resistant for fluconazole and tested agricultural azoles. By WGS analysis we come to know that some strains are sharing the similar genotype as of previously isolated clinical strains while some of strains are different from clinical strains in respect of single nucleotide polymorphism analysis.

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12. YADAV (Suman)
Deciphering the Role of Bisphenol A in the Pathophysiology of PCOS and its Immunomodulatory Effect on Fertility.
Supervisor: Prof. Rita Singh
Th 28529

Abstract

Bisphenol A (BPA) is an endocrine-disrupting chemical present in plastics, food packaging, and other consumer products. It interferes with hormonal regulation, potentially contributing to reproductive disorders such as polycystic ovary syndrome (PCOS) and infertility. BPA causes conditions like increased androgen levels, insulin resistance, metabolic dysfunction, inflammation, menstrual irregularity, and subfertility/infertility. As BPA exposure increases due to plastic use, adolescents and women are at substantial risk for various comorbidities including obesity, type II diabetes, infertility and endometrial dysplasia. This study aimed to examine the role of BPA in initiating aggregation of proteins in the follicular fluid of the ovary. The findings showed that BPA has the potential to aggregate apolipoprotein A1 in mouse and human follicular fluid, leading to increased BPA levels in the follicular fluid of women with PCOS. The exact mechanism or pathway of BPA in protein aggregation remains an area of research and future studies. The study also examined the immunomodulatory effect of BPA on uterine endometrial T cells (Tregs and Th17) and its impact on reproductive and overall health. Chronic oral exposure to a low concentration of BPA during adulthood leads to dysregulation of Tregs and Th17 cells, resulting in uterine hyperplasia and infertility. Targeting the Th17/Treg cell axis by modulating its function may have therapeutic potential in the treatment of PCOS and IVF/infertility. In conclusion, BPA exposure has been linked to reproductive disorders and menstrual irregularities, which could contribute to the etiology of PCOS and infertility. Additionally, a questionnaire-based study found a connection between BPA exposure and the onset of PCOS/PCOD in adolescent girls experiencing menstrual irregularities and excess androgens.

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1. To investigate the role of BPA in causing ovarian defects in mice and human follicular fluid 2. Deciphering the immunomodulatory effect of BPA on uterine endometrial T cells (Tregs and Th17) and fecundity 3. Menstrual Irregularities in Adolescent Girls and Correlation with the Extent of Exposure to Plastics. Summary and Conclusions. Supplementary Data. References and Publications.

13. YASHANKITA

Histone H3 Dynamics During Lymphoma Progression: A Study on Proteolysis, Modifications, Extra-nuclear Histone H3 and Chromatin Reorganization in Murine Model.

Supervisors: Prof. Rita Singh, Dr. J. S. Purohit and Dr. M. M. Chaturvedi

Th 28530

Abstract

In addition to the typical nuclear localization of histones, free extranuclear histones (ENHs) in the cytosol as well as vesicle-bound histones have been reported in a variety of clinical instances, including cancer. In this study, the presence of ENHs is explored in the tumor microenvironment (DL cells) and in the systemic microenvironment (peritoneum, blood, liver, and spleen) of the DL mice. The nuclear localization of H3 was observed in the early stages of tumor in DL mice (liver, WBCs, peritoneum, spleen and DL cells), by using immunocytochemistry and immunohistochemistry studies. However, in late tumor stages of the DL mice, the histone H3 could be detected in the cytoplasm in addition to the usual nuclear localization (WBCs, peritoneum, spleen and DL cells). Additionally, using Mitotracker-Red labelling and western blotting it was observed that the histone H3 could be probed in the ascitic fluid and DL cells of the late tumor mice, suggesting the mitochondrial and exosomal sequestering of ENHs, respectively. The appearance of ENHs is generally associated with the disruption of peripheral heterochromatin (PH). Hence, using transmission electron microscopy (TEM) the PH organization in the DL cells revealed a progressive decrease in the peripheral electron-dense region. Further, immuno-TEM labelling of the DL cells with core-H3, demonstrated a progressive open chromatin conformation (decompaction of PH). Furthermore, using immunocytochemistry of the DL cells, a progressive decrease in the H3K9me3 and H3K27me3 marks and an increase in the pan-acetylated H3 marks with correlated increase in the nuclear blebbing/micronuclei in the DL cells was observed. Western blotting using anti-H3 antibodies demonstrated absence of any cleavage of histone H3 in the DL cells, though the histone H3 specific protease (H3ase) reported by our group was localized to the nuclei of DL cells, suggesting no role of histone H3 cleavage in the chromatin decompation in lymphoma mice model.

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1. Introduction 2. Materials and Methods 3. Results 4. Discussion 5. Summary 6. Conclusion. References and Publications and Conferences.