CHAPTER 7

BIOMEDICINE

Doctoral Theses

031. ANAND (Prachi)
Biochemical Investigations on the Antidiabetic Effect and Mechanism of Action of Cinnamomum zeylanicum and Brassica nigra in Experimental Diabetes.
Supervisors : Prof. Ramesh Chandra and Dr. Vibha Tandon
Th 16884

Abstract

Develops an effective and safe oral antihyperglycemic drug from Brassica nigra and Cinnamomum zeylanicum. Comprehensive studies with their different solvent extracts were carried out in the present work.

Contents

032. BENGANI (Hemant)
Analysis and Validation of Cis-Acting Elements Involved in Chromatin Mediated Global Regulation of Gene Expression.
Supervisor : Prof. Vani Brahmachari
Th 16882

Abstract

Describes the identification of novel motifs and cis-acting elements for the sites of interaction for PcG and TrxG of proteins and their functional analysis. To the best of our knowledge this is the first report on identification of human PRE/TRE. This

would pave way to the identification and validation of other human PRE/TREs and open new doors to mechanistic understanding of PcG/TrxG dependent regulation.

Contents

1. Introduction. 2. Mining the human genome for novel motifs and cis-regulartory sequences involved in chromatin mediated gene regulation. 3. Validation of PRE/TRE like function of cis-elements from human genome with Drosophila melanogaster as in vivo assay system. 4. CE-PIK2B : A novel cis-regulatory element from human genome involved in PcG/ TrxG mediated gene regulation. Bibliography and Appendices.

033. BHATIA (Shipra)
Search for Novel Components of Epigenetic Regulation in Human Genome : Functional Characterization of INO80, a Chromatin Remodeling Protein.
Supervisor : Prof. Vani Brahmachari
Th 16881

Abstract

The result strongly suggest a novel, yet unidentified role of the INO80 complex in regulation of developmental patterning. These results thus add substantially to the understanding of the role of INO80 complex, which is the most-recently characterised and highly evolutionarily conserved member of the SNF2 family of chromatin remodelers. Simultaneously, analysis of the role of the DNA-binding domain of INO80 suggests the possibility of functioning of INO80 as a dual function protein at a subset of INO80 target sites. There is a distinct possibility that INO80 has a crucial role to play in the transcriptional regulation of key developmental regulators, ast least in a subset of which it could behave both as a chromatin remodeler (via the helicase domain) and a recruiter of the regulatory complex (via DBINO domain).

Contents

1. Introduction. 2. Prediction of INO80 as a novel trans-acting factor of cellular memory module. 3. Validation of the predicted role of INO80 in developmental regulation. 4. Identification and validation of INO80 binding sites ont he genome of Homo sapiens and drosophila melanogaster. Bibliography and Appendix.

034. CHOWDHURY (Joyita)
Biological Evaluation of Quinazolinone Derivatives on Cholecystokinin-B Receptor Expressing Cell Lines.
Supervisor : Dr. Madhu Chopra
Th 16887

Abstract

Describes transfection of the CCK-B/Gastrin Receptor cDNA cloned in pcDNA3.1 topo vector; evaluation of the affinity of the quinazolinone derivatives for CCK-B/Gastrin receptor by competition with radioligand [^{125}I]-BH-CCK-8. Studies the localization of CCK-B/Gastrin receptors transfected in NIH-3T3 cells and examine the receptor internalization using fluorescent probe. Also studies the expression of CCK-B/Gastrin Receptor in tumor cell lines of various origin. Checks the antiproliferative effect of quinazolinone derivatives on Pancreatic cancer cell line MiaPaCa-2.

Contents

035. KUMARAN (D)
Investigation of Regulatory Role of Cholinergic System on Inflammation and Apoptosis in Murine Model of Global Cerebral Ischemia.
Supervisor : Dr. Anju Katyal
Th 16662

Abstract

The experimental studies that global cerebral ischemia mediated neuronal inflammation and apoptosis lead to delayed death, cholinergic hypofunction and spatial and associative memory impairments. Global cerebral ischemia also alters the indivisuals cholinesterases activity, increased the HMGB-1p expression and elevates the PARP-1 activity in hippacampus after 8 days ischemia/reperfusion. In addition to the better memory enhancing property, this study also reveals potential anti-inflammatory and anti-apoptotic effects of aholinergic agents like rivastigmine, galantamine and choline during global cerebral ischemia. Besides the acetylcholinesterase inhibitory activity, rivastigmine is found to inhibit butyrylcholinesterase activity while galantamine has allosteric modulatory effect on α7nicotinic receptor. Similarly choline is

specific agonist of α7nicotinic receptor as well as precursor for the acetylcholine synthesis. Hence it is difficult to predict which specific properties of these molecules are responsinle for the observed neuroprotection. Finally the experimental work also adds little knowlege to the existing scientific facts that targeting α7nicotinic receptor may be a potential therapeutic horizon for the treatmetn of demetia and neurodegeneration during ischemia.

Contents

1. Introduction. 2. Review of literature. 3. Scope of the work. 4. Objectives of the work. 5. Materials and methods. 6. Results. 7. Discussion. 8. Summary. 9. Conclusion. Bibliography.

036. MARYAM IMAM
Structural ans Immunological Characterization of Merozoite Surface Protein 3 of Plasmodium Falciparum.
Supervisors : Dr. Akhilesh K. Verma and Prof. V. S. Chauhan
Th 16664

Abstract

The study along with expression of full protein, designed turncated N-terminal MSP3 (PfMSP3N) which includes 70 amino acid regions present in MSP3 sequence which is responsible for maximum ADCI activity. Produces large amount of soluble PfMSP3F and PfMSP3N proteins. For the study, both the proteins, PfMSP3F and PfMSP3N were structurally characterized. Attempts to demonstrate the immunological relevance of the truncated fragment when compared with full protein. Immunoefficacy of these two antigens was carried out by using three adjuvants, alum, CFA/IFA and monranide 720.

Contents

1. Introduction. 2. Review of literature. 3. Materials. 4. Immunological characterization of PfMSP3. 5. Structural characterisation of PfMSP3. 6. Interaction study of PfMSP3 with heme. 7. Antimalarial drug screening. Bibliography.

037. MATHUR (Vidhi)
Molecular Analysis of Differential Regulation of Homologous Chromosomes in Relation to Genomic Imprinting.
Supervisor : Prof. Vani Brahmachari
Th 16663

Abstract

Examines the unusual chromatin organization i.e. nuclease resistant chromatin (NCR) and the associated attributes of male specific heterochromatization in mealybugs. Investigates further into the nature of the sequence elements presents in the mealybug genome that may have some consequence on the differential regulation of homologous chromosome in this system. The trans acting factors such as proteins are expected to play a role in organising the paternal genomes differentially. Attempts to study the post-translational modification on histone tails associated with the differentially organised mealybug genomes and other non-histone proteins interacting with the chromatin.

Contents

038. PATEL (Achchhe Lal)
Development of a Diagnostic Assay for Detection of Chlamydia trachomatis and Characterization of Chlamydial Protein Pkn1 as a Potential Immunogen.
Supervisor : Prof. Daman Saluja
Th 16883

Abstract

Evaluates clinical performance of the in-house PCR and comparison with the Roche Amplicor MWP kit. Studies stabilization of PCR reagents at 4^0C. Describes development of a visualized assay for detection of C. trachomatis.

Contents

039. RAKESH KUMAR

Molecular Mechanism of Demethoxycurcumin-induced Chemoprevention of Glioblastoma Multiforme (GBM) in Human Glioma U87 Cells, a Cell Culture Model.

Supervisor : Dr. Pratibha Mehta Luthra

Th 16880

Abstract

Reveales a significant contribution in understanding the molecular events involved in curcuminods-induced apoptosis in human glioma U87 cells. C2 exhibited significant apoptosis amont all the curcuminods. C2-induced Bcl-2 down-regulation and inhibition led to cell cycle arrest in G2M phase and ROS generation in glioma U87 cells. Significant decrease int he GHS level in C2 treated U87 cells, indicated that decrease in GSH elvel was due to rapid increase in ROS production. The activity of cellular catalase increased in C2 trated cells was not enough to neutralize the ROS generation, causing sifnificant loss of $\Delta\psi m$, and facilitated the significant release of cytochrome c from mitochondria to cytosol. Cytochrome c once released int he cytosol initiated a cascade of events involving activation of caspase-9 and caspase-3 and finally apoptosis in glioma U87 cells. Bcl-2 was not down-regulated in HEK293 cells hence insignificant ROS production was found as compared to U87 cells. Cellular GHS level and catalose activities increased significantly, enough to neutralize the ROS generated. Hence C2 exhibited insignificant apoptosis in HEK293 cells.

Contents

040. SAMEENA ALAM

Anticancer Activity of a Medicinally Important Plant 'Acacia Catechu'.

Supervisor : Dr. Manisha Tiwari

Th 16661

Abstract

Suggest that among different bark extracts of the plant the methanolic extract was found to have maximum cytotoxic potential against oral cancer cell line. Among different bark extracts of the plant methanolic extract was found to have maximum cytotoxic potential against oral cancer cell line. The death in the cancer cell line is caused due to apoptosis and reduction in the COX-2 activity. Cancer cells have the property to migrate of metastatize. The methanolic extract inhibited the metstatic potential of the cancer cells. The extract showed antioxidant potential. The active principal isolated from the methanolic extract has a remarkable cytotoxic activity. Therefore concludes that the plant Acacia catechu does not cause oral cancer infact it cures oral cancer and could be used to treat against diseases caused due to oxidative stress as well as cancer.

Contents

041. SANDEEP KUMAR
Molecular Interaction of Adenosine A2A Receptor with Anti-Parkinsonian Agents.
Supervisor : Dr. Pratibha Mehta Luthra
Th 16886

Abstract

Reveales a significant contribution in understanding the molecular events involved in $A_{2A}R$ and its selective antagonists. Putative identification of PMNYM motif perhaps involved in the dimerization/oligomerization of $A_{2A}R$ has been explored using in silico tools (Luthra et al., 2007). Further observed that blockade of $A_{2A}R$ with SCH 58261 leads ot the large elevation in $[Ca^{2+}]_i$, due to enhanced release of IP1 in the cells. Incresed intracellular Ca^{2+} ions diminish cAMP accumulation, which in turn led to the inhibition of PKA avtivity. Demonstrated that inhibition of cAMP accumulation is caused due to elevated $[Ca^{2+}]_i$. Swim test as a new method to evaluate haloperidol-induced motor disability in animal models of PD has been established. Evaluation of dopamine levels, GSH levels and SOD activity in SCH 58261, L-dopa and caffeine pre-treated,

haloperiodol-induced mice provides their significant role in preventing striatal neurons from oxidative stress.

Contents

1. Introduction and review of literature. 2. Identification of pmnym motif as possible $A_{2A}R$ olifomerization site present in TM 5 Domain. 3. Investigation of signaling mechanism mediated through $A_{2A}R$. 4. Establishment of in vitro radioligand binding methods and in vivo model of parkinson's disease. Bibliography

042. SRIVASTAVA (Rakhi)
Screening and Isolation of Active Principles from Boerhaavia Diffusa as Potential Anticancer Agents and theirMechanistic Study.
Supervisor : Prof. Madhu Chopra
Th 16665

Abstract

Isolates and screen anticancer metabolites from Boerhaavia diffusa. Boerhaavia diffusa ethanolic crude root extract was cytotoxic against Hela cells and U-87 cells whereas no significant activity in hep 3B, HCT-15, MCF-7 and NIH3T. Cell type antiproliferative specificity is observed in B. diffusa ethanolic crude root extract. Isolates a rotenoid named boeravinone F from the ethanolic root extract of B. diffusa through various stages of purification. The structure was established with the help of various spectroscopies. The structure of the known compound was deduced by comparing their spectroscopic data to those reported in literature. Cell viability assay and morphological analyses showed that BDF 5 significantly inhibited HeLa cells proliferation in a time dependent manner. Cell viability assay and morphological analyses showed that sitosteryl oleate (BDPT-3) significantly inhibited U-87 cell proliferation in a dose-dependent manner. p53 expression was not found to be changed whereas cells underwent apoptosis following exposure to sitosteryl oleate (BDPT-3). In the case of the cells used during the present study, it is possible that the effect of BDPT-3 was independent of p53. Results suggest that the sitosteryl oleate (BDPT-3) induced apoptosis by shifting the Bax/Bcl-2 ratio in favour of apoptosis.

Contents

1. Introduction and review of literature. 2. Extraction and

screening of boerhaavia diffusa, oxalis corniculata and hibiscus rosa sinesis for cytotoxicity. 3. Isolation, purification and characterization of active principles from plant boerhaavia diffusa. 4. Inhibilation of human cervical cancer cell growth by boerhaavia diffusa fraction 5 (BDF 5) through S-phase inhibilation. 5. Analysis of apoptosis inducing effect of sitosteryl oleate (BDPT-3) isolated from boerhaavia diffusa in human glioblastoma (U-87) cells. 6. Summary. Bibliography.