CHAPTER 5

BIOCHEMISTRY

Doctoral Theses

01. KAUR (Simran)
Effect of Immunomodulation on Radiation Induced Inflammation and Damage.
Supervisor: Dr. Alo Nag
Th 24345

Contents

1. Introduction 2. Review of Literature 3. Radiation 4. Aims and objectives 5. Material and methods 6. To study the role of PPARG in radiation exposed condition and the mechanism underline 7. To study the role of PPAR gamma in radiation induced inflammation and late effects 8. To decipher the role of immunomodulatory cytokines in radiation scenario and mechanism underlined 9. To combine the cytokines in order to achieve better radioprotection and combat radiation induced inflammation 10. Conclusion and future prospective. Bibliography

02. MANOJ KUMAR
Studies on Erythrocyte Membrane Protein Profile and Oxidant and Antioxidant Status Of Blood in Bronchial Asthma .
Supervisor: Prof. S.K. Bansal and Prof. Rajendra Prasad
Th 24942

Abstract
(Not Verified)

Asthma is a chronic inflammatory airways disorder. Several cells including erythrocytes participate in inflammatory response. Erythrocytes are constantly exposed to oxidative stress, which can damage them structurally and impair their functions. The protein profile of cells changes in diseases. Therefore, in the present study, changes in protein profile of erythrocyte membranes and their correlation with oxidative stress were assessed to understand their role in the disease.Plasma and erythrocytes of asthmatic patients and healthy controls were separated from blood. Protein profile of erythrocyte membranes was determined by SDS-PAGE, 2DGE and LC-MS/MS. The protein-protein interactions (PPIs) and molecular functions of various proteins and glyceraldehyde-3-phosphate dehydrogenase (GAPDH) were assessed. Molecular dynamics simulation models of GAPDH of healthy subjects and asthmatic patients were generated. Oxidants in plasma and antioxidants in erythrocyte lysates were assessed. Correlation of GAPDH with severity of disease and oxidative stress parameters was determined.The results show quantitative and qualitative differences in protein profile of asthmatics and healthy subjects. Some proteins expressed only in asthmatics. Some proteins were upregulated or downregulated in asthma, of which some are known to play significant role in oxidative stress and inflammation. Some proteins had post-translational modifications (PTMs) and showed phosphorylation and/or acetylation, present/ absent in asthma, or active asthmatic state or in remission. The PPIs showed GAPDH as the first shell of interactors, which in asthmatics

interacted with more number of proteins than healthy subjects.Our results show that there is significant correlation of GAPDH with forced expiratory volume in one second in mild persistent and moderate persistent asthma and parameters of oxidative stress, suggesting that increase in GAPDH is associated with decrease in airway obstruction and decrease in various antioxidants. Hence, role of GAPDH and other proteins needs to be explored further, which had been differentially expressed and phosphorylated and/or acetylated in asthma.

Contents

1. Introduction 2. Review of literature 3. Aims and objectives 4. Material and methods 5. Results 6. Discussion 7. Summary and conclusion 8. References and appendix.

03. PODDER (Avijit)
Computational Studies of Drug Targets in Dopaminergic System Implicated in Neurological Disorders.
Supervisor: Dr. N. Latha
Th 24346

Abstract
(Verified)

Dopamine receptors (DRs) belong to the family of G protein-coupled receptor (GPCR) that bind to the neurotransmitter dopamine. DRs are widely expressed in the central nervous system and mediate a number of diverse biological and cellular processes. Till date, research has primarily focused on developing drugs for DR family as malfunctioning in downstream events of these receptors are well reported in complex brain disorders like Schizophrenia and Parkinson's disease. Despite huge efforts being done worldwide, identification of appropriate drug targets for neurological disorders has not been fruitful. Instead of performing functional validation of each of the lead signals from high-throughput association studies, effective computational studies to explore the available data will be an alternative choice to proceed for a more confident targeted functional validation which will save both the resources and the time.This thesis entitled "Computational Studies of Drug Targets in Dopaminergic System Implicated in Neurological Disorders" is an effort to understand the complex functionality of brain dopamine receptors in common neurological disorders by studying all five DRs and their interacting protein partners employing comprehensive computational graph theory based protein-protein interaction network (PPIN) approaches. Diverse network analysis strategies have been applied to study the genetic landscape for two distinct neurological disorders (Schizophrenia and Alzheimer's) and to prioritize the candidate proteins as potential therapeutic targets. Lack of crystal structure of several crucial target proteins allowed us to perform computational protein modeling and Molecular Dynamics (MD) simulations to generate refined three-dimensional model of a drug target for further characterization. The effect of genetic mutation on protein structure was also investigated applying rigorous atomistic MD simulations and docking strategies to understand their potential role in neurological disorders. We believe that this study has conclusively brought forward potential therapeutic drug targets for these complex polygenic brain disorders.

Contents

1. Introduction 2. Review of literature 3. Aims & objectives 4. Understand complex interactions of human dopamine receptors and associated protein partners emplaying a protein-protein interaction network (PPIN) based approach and prioritizing candidate drug targets in brain disorders. 4. Generate refined

three-dimensional model of the prioritized candidate drug target and analysis of the impact of genetic mutation through computational protein modelling and molecular dynamics (MD) simulations 5. Identify tissue specific shared network and common drug target in schizophrenia using co-expression network analysis approach 6. Prioritize and characterize the candidate drug target in alzheimenr's using weighted network analysis, molecular modelling and simulations. Summary of conclusion. Appendix and List of publication.