CHAPTER 14

BIOCHEMISTRY

Doctoral Theses

01. LALWANI (Neha)
Understanding Host-Pathogen Interactions of Mycobacterium Tuberculosis.
Supervisor: Dr. Garima Khare
Th 28182

Abstract

Tuberculosis (TB), caused by the etiological agent, Mycobacterium tuberculosis (Mtb), a historic acquaintance of mankind, is an airborne disease that ranks as the world's top infectious disease killer in 2024, and till date it continues to remain a global epidemic. Despite the availability of an effective chemotherapeutic regimen, the heterogeneity of the TB disease, the emergence of drug resistance which often results due to non-adherence to the long treatment periods, toxic side effects related to the therapy, reactivation of latent forms of the disease along with complications associated with HIV-TB co-infection, makes controlling TB a difficult task. Thus, the urgency for the development of newer and safer anti-TB therapies with novel action mechanisms, as well as the identification and validation of molecular targets that are important for the survival or virulence of the pathogen cannot be over-emphasized. The robust mycobacterial cell wall is considered as one of the main virulence determinants of this pathogen. Hence, targeting proteins either associated with the cell wall directly or involved in its biosynthesis, can be thought of as a rational approach. Towards this, the studies detailed in this thesis were focused on the evaluation of the role of three mycobacterial proteins, namely, NagA (N-Acetyl-glucosamine-6-phosphate deacetylase), LprA (a lipoprotein) and SerA1 (3-phosphoglycerate dehydrogenase) in Mtb. Homologous recombination and antisense-based techniques were employed for the generation of Mtb mutant strains. In vitro and in vivo studies were carried out, which demonstrated the importance of these proteins in Mtb survival and virulence. Moreover, we attempted to identify certain host gene signatures that are evoked upon Mtb infection, by employing RNA-Seq technology. Besides, for SerA1, structure-based virtual screening was also carried out to identify novel inhibitors against this essential enzyme, which occupies a central position in Mtb metabolism.

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1.Introduction 2. Review of literature 3. Aims and objectives 4. Results and discussion 5. Evaluation of the role of NagA in the growth and pathogenesis of Mycobacterium tuberculosis 6. Evaluation of the role of lpra operon in the survival and virulence of Mycobacterium tuberculosis 7. Evaluation of the role of sera1 in the growth of Mycobacterium tuberculosis and identification of novel inhibitors against it 8. Summary and Conclusions. Appendix and Publications.

02. PANDIT (Mansi)

Immunoinformatics Approaches to Understand Molecular Basis of Allergy.

Supervisors: Dr. Nandita Narayanasamy and Dr. Latha Narayanan

Th 28183

Abstract

Allergies refer to chronic inflammatory diseases such as rhinitis, asthma, eczema, urticaria, angioedema which currently affects nearly 30-40% of the world population. Presently, more than 25% of Indian population is sensitized with different forms of allergens such as pollens, moulds, foods, mites, insects, pets, animal dander and drugs. Despite such high prevalence, treatment methods mainly include allergen avoidance, use of antihistamines, corticosteroids, NSAIDs and limited use of sublingual/subcutaneous therapy. This thesis entitled "Immunoinformatics Approaches to Understand Molecular Basis of Allergy" is an effort to comprehend underlying mechanisms of allergy with the aim of designing potential therapeutic interventions. The study employs use of various computational approaches such as structure prediction, protein-protein docking, molecular dynamics simulations, in silico mutagenesis, epitope prediction, allergen prediction among others to gain insights on structural and binding characteristics of allergens. Pollen allergens from Birch tree, Parthenium hysterophorus weed and pectate lyase allergen family have been focused upon for the design of potential hypoallergens and/or vaccine candidates. The study also deals with identification of prevalent allergen sources from clinical patient samples by analyzing Skin Prick Test and allergy questionnaire data. Furthermore, immunochemical techniques have been utilized for determining the presence of pollen allergies in clinical samples. We believe that the outcomes of this study will help in design of therapeutic interventions for better management of allergy.

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