HOST PATHOGEN INTERACTIONS IN ALLERGIC AND INVASIVE FUNGAL DISEASES: DIAGNOSTIC AND THERAPEUTIC IMPLICATIONS

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Fungal diseases are emerging as public health problem especially with increasing incidence of HIV, tuberculosis, cancers and use of immunosuppressive drugs. The incidence of *Aspergillus* induced allergic and invasive forms of Aspergillosis is on the rise in the recent past. The ubiquitous occurrence and universal distribution of this opportunistic airborne fungi attracted a large number of researchers to undertake multidisciplinary and molecular approaches to study the host-pathogen interactions.

Aspergillus specific cellular and humoral immune responses are found in many clinical forms of the pulmonary aspergillosis. These responses have no role in protection and are implicated in immunopathogenesis. Allergens and antigens of *A. fumigatus* induce type I and type III hypersensitivity reactions and the cellular immune response is skewed towards Th2 type of responses. Hyposensitisation is contra indicated in *Aspergillus* induced disorders and immunotherapy has not been successful in prevention.

It is also interesting to note that exposure to fungi cause allergic disease in atopic individuals and some of the immunocompetent hosts. Hence the basic nature of the factors contributing to host's innate immune mechanisms need to be investigated.

Indigenous efforts on molecular characterization of immunodominant allergens and antigens of *Aspergillus* species through biochemical, immunological and molecular biological studies resulted in development of sensitive and specific immunodiagnostic assays and molecular probes for Aspergillosis. Evaluation of synthetic epitopes helped

in their use for immunodiagnosis of Aspergillosis. These immunossays can be further developed into simple user friendly formats usable in clinical and pathological laboratories. Serodiagnostic methods are generally based on antigen load and host's immune competence. Highly sensitive assays are required for detection of antibodies in low concentrations. Luminescent immuno assay is an example of such a sensitive immunoassay.

Detection of antigen is one of the valuable diagnostic criteria in immunosuppressive conditions. Molecular probes are of great relevance and importance in such cases. Genetic susceptibility of the host to the environmental factors is being explored for predictive diagnosis of allergic and infectious diseases. A beginning has been made in this direction for important clinical forms (allergic and invasive forms) of the fungal disease Aspergillosis.

Lung being the focus of many allergic respiratory pathogens and surfactant proteins being major contributors to the maintenance and function of lung tissues, a study has been conducted on biochemical interactions of lung surfactant proteins and the fungal glycoprotein allergens and antigens. Besides, total lung surfactant has been used in therapy of various allergic disorders. It is well established that the lung surfactant system maintains appropriate surface tension in alveoli during inspiration and expiration and is also involved in protection against pulmonary pathogens.

Lung surfactant proteins A and D play an important role in innate immunity in the lungs by

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binding to carbohydrate moieties present on a range of microbial pathogens via their multiple C type lectin domains. Major aspects studied include specific antibody binding, histamine release, phagocytosis, neutrophil oxidation and oxidative burst etc., in in vitro cell culture system. Significant modulation in the above parameters resulting upon interactions of lung surfactant proteins with conidia of *A. fumigatus* indicated possible involvement of lung surfactant proteins in innate immune mechanisms in anti fungal defense. Therapeutic value of the lung surfactant proteins was examined in murine models of allergic bronchopulmonary aspergillosis and invasive

aspergillosis and the results are suggestive of their use in therapy. The genes of lung surfactant protein may show polymorphism/nutations in susceptible individuals.

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