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Development of Comprehensive Online Database Model for Genes Responsible for Asthma

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ABSTRACT

Asthma is a complex disease associated with bronchial hyperreactivity and atopy, making asthma a disease with a phenotype that has been clinically difficult to define. Despite intense research, prevalence of asthma remains relatively high. Epidemiologic studies provide evidence that the interaction of multiple genetic and environmental factors contributes to the causation of asthma. To date, more than 120 candidate genes of the innate and adaptive immune systems have been associated with asthma or atopy-related phenotypes. We have created a comprehensive online tool model for those people who work exclusively on asthma research and the tool will enhance the way they work by simplifying the whole process of accessing several databases at several instances. As a fundamental requirement all the genes that are involved in causing Asthma can be included in the database and can be retrieved at any moment if needed.

Keywords: Asthma, Genetic factors, Web based tools, Bioinformatics.

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INTRODUCTION

Asthma is a phenotypically heterogeneous inflammatory airway disease associated with intermittent respiratory symptoms, bronchial hyperresponsiveness, and reversible airflow obstruction. It is a common condition that has increased in prevalence throughout the world over the past 30 years. Sophisticated paradigms depict asthma as a disorder of complex genetic and environmental interactions that affect the developing immune system and ultimately result in the episodic release of pro-contractile mediators, including leukotrienes and prostaglandins, causing susceptible individuals to wheeze. In susceptible individuals this inflammation causes recurrent episodes of wheezing, breathlessness, chest tightness, and cough, particularly at night or in the early morning (1-4).

The identification of novel genes and associated pathways delineates new pharmacologic targets for developing therapeutics (5,6). Asthma genetic research may improve diagnostics that could identify susceptible individuals allowing early life screening and targeting of preventive therapies to at-risk individuals. Asthma pharmacogenetics can subclassify disease on the basis of drug-metabolizing polymorphisms and genetic modifiers, permitting targeting of specific therapies (7). Such data also may determine the likelihood of an individual's responding to a particular therapy and permit the development of comprehensive individualized treatment plans. Genetic factors, predominantly atopy and parental history of asthma, are key components in the development of asthma (8,9). Asthma and atopy are related conditions most likely involving multiple genes that interact with each other and the environment.

Epidemiologic studies provide evidence that the interaction of multiple genetic and environmental factors contributes to the causation of asthma (6,8). Patients who have asthma vary in age of onset, course, sensitivity to specific environmental precipitants, and response to therapy. Consequently, the relative contribution of genetic factors also may vary considerably among patients. The prevalence of asthma has risen dramatically in the past two decades, suggesting that environmental risk factors have a key role. Viral respiratory infections, primarily those caused by respiratory syncytial virus, are a significant risk factor for the development of childhood wheezing in the first decade of life.

Asthma genetics uses genetic mapping techniques to localize gene loci to asthma and physiologic studies followed by positional cloning to identify genes that affect the disease process (10,11). Various mapping techniques have identified several genes and chromosome regions associated with asthma. Different populations of patients might have different asthma profiles, and the association of specific genetic markers might be limited to specific traits and groups of patients. The number of candidate genes and implicated chromosomal regions remains large (10,11). Position cloning is used to identify complex trait susceptibility genes (10-12). The most frequently studied chromosomal regions that may harbour asthma and/or atopy susceptibility genes are on chromosomes 11q, 5q and 12q. After determining linkage between asthma and a chromosomal region, the next challenge is to screen this region for candidate genes.



A candidate gene for asthma has to meet four criteria: (i) the gene product must be functionally relevant to asthma; (ii) mutations within the gene must alter the function of the gene; (iii) asthma needs to be linked to the chromosomal region harbouring the candidate gene; and (iv) asthma has to show association with different alleles of this candidate gene. To date, a number of candidate genes for asthma and atopy have been studied. Development of an online tool model for genes responsible for Asthma provides information about the nucleotide sequences, information about genes like gene_id, gene name, genomic region, transcript product, genomic context, general gene information, and similarity search details. Therefore, a web interface using bioinformatics tools will be easy in accessing these data.

MATERIAL AND METHODS

Collection of genes responsible for asthma and Database creation

Information about each of these genes was collected from various sources. Information consisted of genomic region, transcript product, genomic context, general gene information, protein information, protein interaction and PDB files for each gene are collected and stored in the database. Genes responsible for asthma were collected from Gene Bank and then nucleotide sequence was retrieved in FASTA format. These sequences were saved in single line. Using the sequences gene name, gene id were obtained. The gene id and the corresponding nucleotide sequences were stored in the database. MySQL is used to store the data. MySQL is a relational database management system (RDBMS) that runs as a server providing multi-user access to a number of databases. Free-software projects that require a full-featured database management system often use MySQL. Such projects include (for example) WordPress, phpBB, Drupal and other software built on the LAMP software stack.

Designing of web interface to access the data

Web pages were created using Java script, Servlet and the database is connected to the web page using J/ODBC connection. The front end was created using Java script which is an object-oriented scripting language used to enable programmatic access to computational objects within a host environment. Although also used in other applications, it is primarily used in the form of client-side JavaScript, implemented as part of a web browser, providing enhanced user interfaces and dynamic websites. JavaScript is a dialect of the ECMAScript standard and is characterized as a dynamic, weakly typed, prototype-based language with first-class functions. JavaScript was influenced by many languages and was designed to look like Java, but to be easier for non-programmers to work with.

A Servlet is a Java class which conforms to the Java Servlet API, a protocol by which a Java class may respond to http requests. Thus, a software may use a servlet to add dynamic content to a Web server using the Java platform. The generated content is commonly HTML, but may be other data such as XML. Servlets are the Java counterpart to non-Java dynamic Web content technologies such as CGI and ASP.NET. Servlets can maintain state in session variables

across many server transactions by using HTTP cookies, or URL rewriting. A Servlet is an object that receives a request and generates a response based on that request. The servlet API, contained in the Java package hierarchy javax.servlet, defines the expected interactions of a Web container and a servlet. A Web container is essentially the component of a Web server that interacts with the servlets. The Web container is responsible for managing the lifecycle of servlets, mapping a URL to a particular servlet and ensuring that the URL requester has the correct access rights.

RESULTS AND DISCUSSION

In our working model, home page was set up by including registration page, gene and protein information related to Asthma. The database created on asthma contains all the genes that are involved in causing this atopy. Information about each of these genes were collected from various sources are in stored in the database (Fig 1 & 2). The developed model will exhibit Information consisting of genomic region, transcript product, genomic context, general gene information, protein information, protein interaction and PDB files for each gene (Fig 3). This is a comprehensive tool for researchers. It will help them to retrieve information, on any gene involved in asthma whenever required. Accessing the data in the front end is made to the user through web page. This makes access of data easier and faster. One can get any information by just entering the gene name or ID. Also the corresponding mRNA and protein sequence can be retrieved, which is important to the researchers.

The etiology of asthma is likely multifactorial. Genetic factors may control individual predispositions to asthma. Genetics may also be associated with responses to medications. Genetics alone cannot account for the significant increases in prevalence, as genetic factors take several generations to develop, and asthma and atopy are not always co-inherited. Several environmental or lifestyle factors have been implicated in this disease. The genetics of asthma has become a promising new field of research. To date, several candidate genes have been identified (13-15). The recent identification of multiple linkages between asthma and different chromosomal regions represents a first step towards the identification of these asthma genes.

Interactions of genetic and environment factors are pivotal to determine asthma development (8,9,16,17). To date, more than 120 candidate genes of the innate and adaptive immune systems have been associated with asthma or atopy-related phenotypes. Some of the factors involved in the induction of asthma, are infections and aeroallergen exposure environmental tobacco smoke (ETS) exposure (18). Among them, respiratory infections have been intensively investigated. As one of the highly risky environmental factors, infections in predisposed individuals can promote asthma development and exacerbations and/or prolong symptoms.

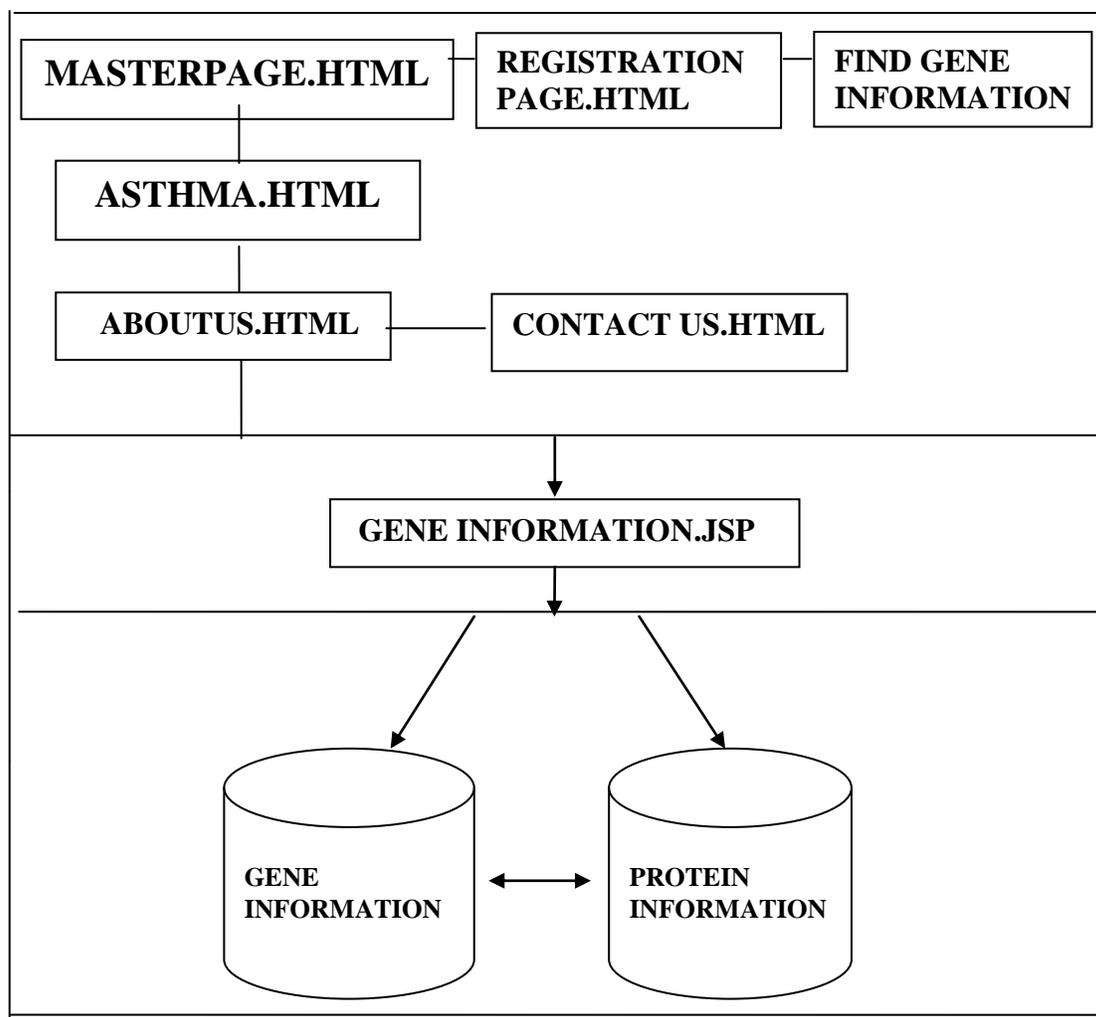


Figure 1 : Developing web based tool model by collecting preliminary information such as genes and proteins information for Asthma, Page and HTML setup

Although the claims for immediate impact of genomics have sometimes been overstated, the ultimate consequences of the integration of genomics into medical research and practice are likely to be revolutionary. By providing insights into the networks and pathways of biology, genomics has already begun to alter the fundamental understanding of health and disease such as asthma. By providing more sophisticated knowledge of biology at the individual and of disease typology, genomics has already begun to personalize health care. By widening the number of potential drug targets and better identifying those children a specific drug is likely to benefit and those it is likely to harm, genomics already has begun to expand the pharmacotherapeutic regimen. However, in recent years, the procession from linkage to the actual identification of the gene has proved to be difficult. In the coming years, developments in molecular biology and genetic epidemiology may accelerate the process of the identification of genes for asthma and atopy.

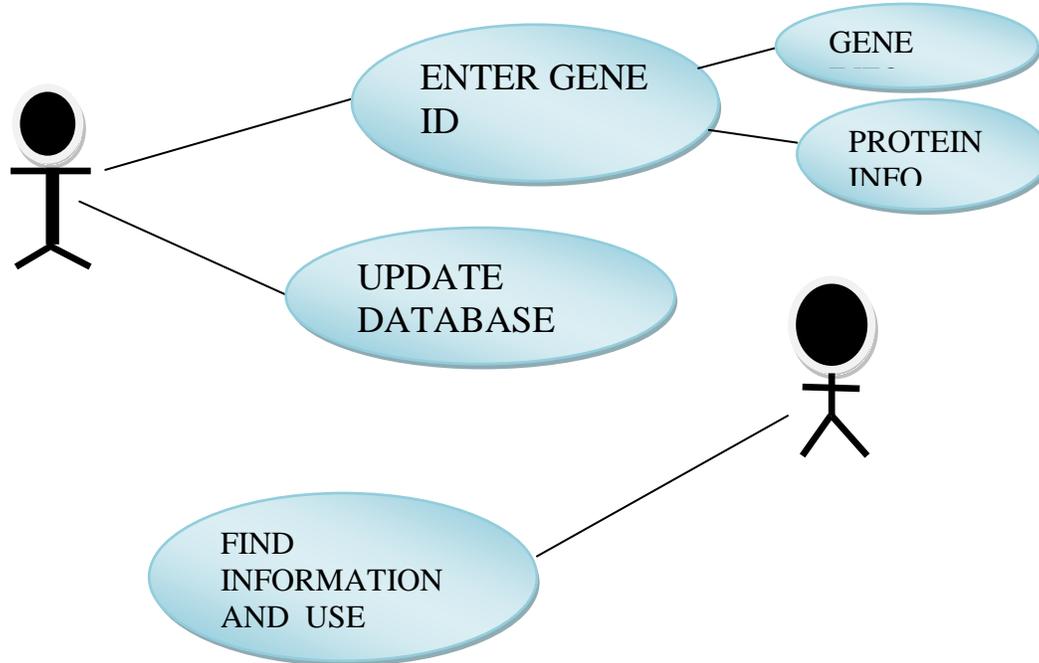


Figure 2 : Allotment of Gene network model to be used by an Administrator and Researcher

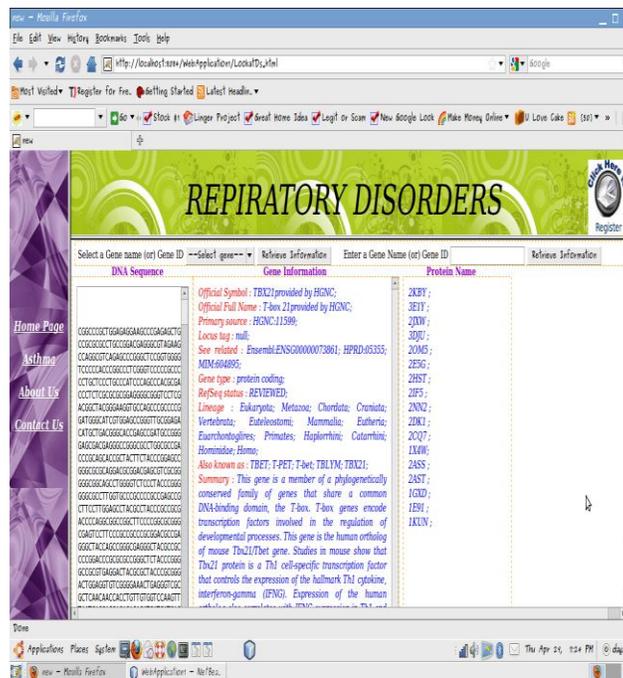


Figure 3: Screen shots showing information of list of Asthma related DNA Sequence, Gene information and Protein Name

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