کارگاه‌های آموزشی مرکز اطلاعات علمی

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اصول تنظیم قراردادها

آموزش مهارت های کاربردی در تدوین و چاپ مقاله
The Iranian Human Mutation Database

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Introduction

More than 20 years have elapsed since the first single base pair substitution underlying an inherited disease in humans was characterized at the DNA level. Disease-associated gene lesions are currently collected and publicized by the Human Gene Mutation Database (HGMD) in Cardiff, locus-specific mutation databases, and to some extent by the Genome Database (GDB) and Online Mendelian Inheritance in Man (OMIM) as comprehensive and up-to-date resources for information on genetic disorders and mutations causing them.1 – 4

The mutation spectrum observed for any gene or disorder will often vary not only between population groups but also between distinct ethnic groups within a geographical region. This is an important extra-dimension reflected in the recent emergence of a new type of mutation depository, namely the National Mutation Databases (NMDBs)5 that serve to enhance awareness among health care professionals, bioscientists, patients, and the general public about the range of common genetic disorders, and can provide essential reference information for the detection of mutations for clinical laboratory settings.

Information on inherited disorders in Iran is not extensive. There are only two detailed studies on the incidence of beta-thalassemia6, 7 and non-syndromic sensorineural deafness.8 But a huge amount of sporadic data are available for more than 100 genetic diseases, such as G6PD, alpha-thalassemia, sporadic breast cancer, infertility, mental retardation, cystic fibrosis, familial Mediterranean fever, etc.

By studying the multiethnic Iranian population (Figure 1), researchers have access to a valuable genetic pool as it has been shown that the mutation spectrum in each region of Iran corresponds to the mutation spectrum in neighboring countries (Figure 2).

Because of its very rich gene pool, Iran has a valuable source of material for the identification of the genes involved in different conditions. In order to promote the human genome study in a collaborative worldwide manner, the Iranian Human Mutation Gene Bank has been established and through this DNA bank many collaborative projects have been started. Presentation of the latest information of such joint-projects will help scientists to follow the progress of such joint projects.

Figure 1. Multiethnic Iranian population. Iran is made up of several ethnic groups, with Persian and Azari making up the majority of the population (51% and 24%, respectively).8 In addition, there is a high degree of consanguinity in Iran.
Establishing the Iranian Human Mutation Gene Bank (IHMGB: www.IHMGD.hbi.ir) was an important advancement toward presenting the latest findings in the area of Iranian genetic disease at the international level and has had a great impact on the mutual exchange of views with centers abroad.9

The Iranian Human Mutation Database (IHMD) was established to collect reported mutations of the Iranian human gene pool and make this information accessible through the internet to achieve the following goals:

- Collection of data regarding reported mutations either published or internationally presented to make them accessible for any interested research groups.
- Prevention of redundant research projects by making the information on ongoing research available to the researchers in Iran.
- Presentation of the latest Iranian genetic achievements at the international level to promote human genome study and to make study opportunities with other countries possible through joint projects.

The basic structure and dynamic webpages were created by computer programming languages DHTML and JavaScript. The database was created using DHTML, JavaScript, ASP, and SQL server machinery.

The website is hosted by Iranian Ministry of Health and Education (HBI) Bioinformatics Center.

The IHMD is now accessible worldwide through the URL http://www.ihmd.hbi.ir. It was indexed in the “Google”, three weeks after introduction. Upon performing a “Google” search using the site keywords “Iranian, Human, Mutation, Database”, the IHMD link comes up as the first link. This also implicates the standard structure of the site.

In addition, in order to make this information available for interested scientists all over the world, the IHDM will be registered and become available through Human Genome Variation Society Website (http://www.hgvs.org/) as an Ethnic and National Variation Database.

In total, 17 pages for users have been designed to make interactive bidirectional information exchange possible; 12 pages and one database file were created to easily store, manage and update the data of the IHMD through data entry pages.

The pages that are accessible by users are:

- Home (main) page
  This is the first page users see using the URL: http://www.ihmd.hbi.ir. Through links provided in the two menus (fixed menu on the top of the page and dynamic side-menu on the right side of the page) users can easily access the different parts of the database. In addition to brief information about this database, there are shortcut links to the information submission form and many other useful and relevant databases such as Human Gene Mutation Database (HGMD), Genome Database (GDB), Online Mendelian Inheritance in Man (OMIM) and Iranian Human Mutation Gene Bank (IHMGB).

- Search facility
  Through this page, the user can search the database for desired data. Information can be retrieved using two different methods:
  1-Search by disease index: users can search for information on disease-causing mutations using the first letter of the disease name.
  2-Search by keyword: users can search the database using keywords in different fields of the database including disease name, gene, mutation name or reference (Figure 3).

Each page has a link to related information in NCBI; by this way users are able to see the required information on disease, gene, and protein.

If the information is not from a published paper (e.g., data presented in an international meeting but not yet published) users will see the word “preliminary” at the end of the reference.

- Information submission form
  Using this form, researchers who study the Iranian population can easily submit preliminary or published data. This information will be sent to the
database maintenance team; after approval, the data will be added to the database. These data should be published in reliable journals or accepted for publishing or in some case, data presented in International congresses; furthermore, the study should have been done on an Iranian population.

- Other pages
  Many other pages have been developed for users including the contact information page, comment page, and useful links page. In these pages, useful information on Iranian universities and research centers, as well as bioinformatic databases/softwares and links to different Iranian websites, are provided for all scientists who want to collaborate with their Iranian counterparts.

- Site statistics
  This facility keeps the users being informed on the latest changes and the number of entries in the database, which is automatically retrieved from the information in the last updated version of the databank. Currently, up to 98 genetic diseases, 138 genes and 415 mutations have been collected with the information on mutation(s) or polymorphism of each gene. References and authors are also listed by the mutation. Before formal announcement, IHMD has had more than 600 visitors since February 2004, of whom 60% were from Iran and the rest were from other countries. So far (August 2006), more than 3000 scientists have accessed this database from different countries such as USA, UK, Poland, France, etc.

- Database Structure and Data Entry Process (Figure 4)
  As this database is the central part of the IHMD, it was designed using the following important criteria:
  1- Easy update process
  2- Prevention of entry of repetitive records and information
  3- Security, speed and possibility of upgrade

**Important points about using ASP programming**
- Users’ requests are processed on the server and then the results are sent to the user’s computer, so that when information is exchanged between the users and the server, network traffic will be minimized.
- Using the four search fields (Disease, Gene, Mutation and Reference) and keywords, users can limit their search to the desired results and customize the result page.
- Site security is high, because ASP codes can not be seen by users.
- Result pages can be viewed by all browsers because they are in HTML format.
- Cross-database links enable users to have access to the latest information regarding the

**Figure 3.** After executing the search process, all the information on the keyword entered is shown in the following order:

**Figure 4.** The structure of the data entry process; for each disease there are related genes and mutations mentioned in references.

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data they have retrieved from their search by clicking on each item, which directly connects users to the relevant pages in the NCBI database.

Because our bank has a relational database, different parts of the data are entered independently and the program links them together. So each piece of information will be entered only once. This will reduce the database size for quick information retrieval.

This database is capable of handling about one million records. Once we have exceeded this number, we can upgrade to an SQL database.

Discussion

Iran is one of the developing countries with many research centers and ongoing research projects. Preliminary data from these projects cannot be submitted to international databases. The mission of the IHMD is to collect all mutation data on Iranian subjects to provide the opportunity for scientists to consider these data in future research planning.

The IHMD combined with other Iranian databases, such as the IHMGB, provide a valuable resource for the study of genetic diseases in Iranian families. Ultimately, these databases help Iran and other countries around the world to diagnose and prevent genetic disorders.

As Iran has a multiethnic population consisting of Arab, Turkish, Kurdish, Afghani, and Pakistani groups, its gene pool could represent the information on the neighboring countries. The IHMD provides information not only for scientists in the neighboring countries but also for all scientists throughout the world who want to perform research regarding the Middle Eastern populations.

The IHMD has a number of technical advantages, including:

- The IHMD website works independent of the computer monitor resolution. Users can see a whole page width, regardless of the monitor model or resolution, without scrolling to left/right.
- Users are able to see the website using Internet Explorer (version 4 or higher) or Netscape which are the browsers used by more than 95% of users.
- Two dynamic menus are prepared for user pages:
  - The fixed menu is located under the logo; with a tree structure, it is divided into submenus to prevent inconvenient lengthening of the main menu, yet providing direct access to the selected parts of target pages.
  - The floating menu is located on the left side of each page and has the same position even while scrolling down pages. In this way, users have no need to use the fixed menu when they are at the bottom of long pages.
- The page sizes are small (on average 15 kB) for fast downloading.
- All data entry forms are set to accept a special kind of data for increased security.
- The update process is possible without the limitations of time or place. This means that the site can be updated anywhere in the world with minimal requirements.
- Using special computer programming and well-designed data entry, the update process can be done by ordinary operators with no need to employ a computer programmer to keep and update data.

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References

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