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FINAL REPORT 2000/RD/10024, INFORMATION NETWORK FOR IMMUNODEFICIENCIES

The project was started in mid December 2000 and ended on mid December 2002 with the aim of building a comprehensive knowledge base for immunodeficiencies. The service called ImmunoDeficiency Resource (IDR) (<http://bioinf.uta.fi/idr>) provides information on primary immunodeficiencies, rare disorders that affect the human immune system, for different interest groups. Altogether more than 100 immunodeficiencies are known. The knowledge is provided in a user-friendly data service in Internet. All the data in IDR will be validated by experts. All the Member States are involved as well as several non-member countries.

ACTIVITIES

In the project worked scientists and a secretary. Since the project lasted only for two years and we got funding for a secretary from other sources a decision was made to change the balance of the personnel costs to research staff from the original budget. This move was really necessary, because during the project quite a number of new immunodeficiencies and genes related to them were identified and thus also the number of fact files to be generated into the system increased.

February 1-2, 2001 was held a start-up meeting in Tampere, Finland, to which was invited the steering group of the project. In the group there are represented specialists from different fields of immunodeficiencies. The steering group provides ideas and suggestions for the development of the knowledge base. The meeting was very fruitful. The steering group as well as other specialists function as curators for individual diseases to validate all the data and links included in IDR. Another steering group meeting was held on January 31st 2002 in London. The time point and location of this meeting was chosen to match with the meeting of the board of the European Society for ImmunoDeficiencies. Many of the steering group members were also board members of the society and we could save on travel expenses. In this meeting many details of the disease fact files were discussed and finalized.

DISEASE FACT FILES

To collect the information about immunodeficiencies and to distribute the data effectively for different platforms such as desktop computers and mobile devices including mobile phones

we have developed a new way of presenting disease information. Inherited Disease Markup Language (IDML) facilitates systematic description of the immunodeficiency related information (manuscript in preparation). IDML is an extension of XML (Extensible Markup Language) for the distribution and description of documents in Internet. IDML will be freely available.

Altogether 105 fact files are currently available for immunodeficiencies. Fact files are comprehensive collection of information for each individual disease and gene. The files contain plenty of information and numerous links to other services. The fact files function as the basis for the whole IDR system.

IDdiagnostics

The diagnosis of immunodeficiencies can be daunting because similar symptoms may be caused by several disorders. A further complication is that many IDs are rare. Making early and reliable diagnosis is often crucial for efficient treatment of these diseases. Delayed diagnosis and management of IDs can lead to severe and irreversible complications even resulting to the death of the patient. The early or possibly prenatal molecular diagnosis allows enough time for the most suitable management and selection of treatment, which is crucial for the survival of the patient.

The definite diagnostics of IDs depends on genetic and clinical tests since the physical signs may be non-specific, very discreet, or absent. In many cases the diagnosis has to be based on the analysis of genetic defect(s). Due to the rareness of the diseases there are generally not many laboratories analysing a particular disease. IDdiagnostics registry contains two databases, genetic and clinical, which are collected to provide a service for those trying to find quickly the nearest and/or most suitable laboratory conducting IDs testing. It consists of a list of laboratories performing genetic and clinical testing for patients with heritable immunodeficiencies.

The tests are listed into a database available at <http://bioinf.uta.fi/IDdiagnostics>. IDdiagnostics database provides search facilities, which allow users to run text based search queries. Gene test laboratories can be searched by disease name (also alternative names), gene symbol, OMIM code, laboratory, laboratory location and free text. Similar searches are available for clinical laboratories. A search engine makes it easy to find laboratories for certain disease(s), methods and/or geographical locations.

The manuscript for the system, submitted to *Journal of Clinical Immunology* is enclosed.

ImmunoDeficiency Resource

IDR is the core of the knowledge base. It provides links e.g. to the fact files and IDdiagnostics. The service contains several introductory texts. From the IDR one can find

classification and diagnostic criteria on immunodeficiencies. There is increasing amount of genome information: immunodeficiency related genes and their locus on the genome, reference sequences on three levels (genome, RNA and protein), markers etc.

The validation of information on the IDR is of prime importance. The service is maintained with the assistance of Regional Experts and Expert Curators and all data will be validated. Each disease will have its own curators, who are established scientists and experts on this particular field and who go through all the data submitted in IDR. Nurse (INGID) and patient societies (IPOPI) are also included in the selection. The IDR offers tens of thousands of validated links to other sites, which are periodically automatically checked.

The IDR also contains articles, instructional resources, and analysis tools as well as advanced search routines. Extensive cross-referencing and links to other services are available. It is possible to search for any text string or multiple strings with Boolean logic search facility across IDR pages. The IDR pages are extensively hyperlinked to the immunology glossary that contains descriptions for over 1,000 immunological terms.

The IDR immunology section lists collections of immunology related data sources including lectures on immunology and immunodeficiencies. The pages also contain animal models and knock-outs of immunodeficiency related genes. There are several societies related to immunodeficiency research, care and patients. Immunology societies, nurse societies and patient organisations as well as patient pages include further links to other interest groups. Patient pages are usually more personal and often contain patient histories as well as personal experiences of the diseases. Immunology laboratories contain a list of home pages of laboratories that are active in many fields of immunodeficiency research, including diagnosis, treatment and basic research on areas such as genetic analysis, protein structure determination and signal transduction. PubMed search is possible directly by certain disease or gene. Links to immunodeficiency related genomic DNA and amino acid sequences as well as three-dimensional structures of proteins are available.

DATA DISSEMINATION

The immunodeficiency data is constantly updated and immediately distributed. New versions of the different parts of the service are released if not daily at least on weekly basis. The IDR system has obtained a large number of visitors. During year 2002 there were about 60,000 downloads from 50 countries from the service. The numbers of monthly visits nearly triplicated after presentation of the service in European Society for ImmunoDeficiencies meeting on October 2002.

IDR and IDdiagnostics have been presented in a number of scientific meetings either as talks or in posters:

Vihinen, M., Pusa, M., Riikonen, P., Ylinen, T. and Väliaho, J. Beyond mutation databases – Immunodeficiency knowledge base: Immunodeficiency resource. 11th International Mutation Database Meeting, 12.10.2001, San Diego, CA, USA.

Väliaho, J., Riikonen, P. and Vihinen, M. Maintenance and analysis of mutation databases in the Internet. Bioinformatics 2001, 29.03-01.04.2001, Skövde, Sweden.

Väliaho, J. and Vihinen, M. The Immunodeficiency Resource: Knowledge base for immunodeficiencies. Bioinformatics 2001, 29.03-01.04.2001, Skövde, Sweden.

Pusa, M., Väliaho, J., Lehtiniemi, J., Ylinen, T. and Vihinen, M. The Immunodeficiency Resource: Knowledge base for immunodeficiencies. ISMB 2001, 21.07-25.07.2001, Tivoli Gardens, Copenhagen, Denmark.

Väliaho, J. and Vihinen, M. A metadata framework for hereditary diseases using XML-based factfiles. Bioinformatics 2002, 4-7.4.2002, Bergen, Norway.

Samarghitean, C., Väliaho, J. and Vihinen, M. Immunodeficiency diagnostics registry: IDdiagnostics. Xth meeting of the European Society for Immunodeficiencies (ESID), 17-20.10.2002, Weimar, Germany.

Väliaho, J., Piirilä, H., Ylinen, T. and M. Vihinen, M. Immunodeficiency mutation databases (IDbases). Xth meeting of the European Society for Immunodeficiencies (ESID), 17-20.10.2002, Weimar, Germany.

Väliaho, J., Samarghitean, J. and M. Vihinen, M. Primary immunodeficiency information resource in the Internet using XML-based fact files. Xth meeting of the European Society for Immunodeficiencies (ESID), 17-20.10.2002, Weimar, Germany.

Samarghitean, C., Väliaho, J., and Vihinen, M. IDdiagnostics, the primary source of information for genetic and clinical tests on immunodeficiencies. XXIV Tampereen lääkäripäivät, 20-22.3.2003, Tampere, Finland.

Vihinen, M. PID mutation databases. International symposium on primary immunodeficiency diseases, 15-17.8.2002, Debrecen, Hungary.

We have also scientific publications about the service:

Väliaho, J., Riikonen, P., and Vihinen, M. Novel immunodeficiency data servers, (2000) *Immunol. Rev.* **178**, 177-185.

Väliaho, J., Pusa, M., Ylinen, T. and Vihinen M. IDR: The immunodeficiency resource, (2002) *Nucleic Acids Res.* **30**, 232-234.

Samarghitean, C., Väliaho, J. Piirilä, H., Pusa, M. and Vihinen, M. Immunodeficiency information services. *Primary Immunodeficiency Diseases* (Ochs, H. D., Smith C. I. E. and Puck J. M., eds) (in press).

Samarghitean, C., Väliaho, J., and Vihinen, M. Online registry of genetic and clinical immunodeficiency diagnostic laboratories, IDdiagnostics. *J. Clin. Immunol.* (submitted).

Väliaho, J., Riikonen, P., and Vihinen, M. Biomedical data description with XML. Distribution of immunodeficiency fact files – from Web to WAP. (manuscript).

As the large number of visits to the service and contacts, mainly by e-mail, indicate there is really a need for this kind of service. The feedback from users of IDR has been very positive.

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