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Thalassemia on the WEB: from laboratory research to e-dissemination

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The objective of this review is to present and discuss in a comparative manner information and e-products present in the Internet and concerning the research and achievements on β-thalassemia. The aim of the present study is to give readers interested in β-thalassemia the possibility to be informed and/or participate to ongoing initiatives in the field of thalassemia-related research, including diagnosis and therapy.

KEY WORDS: Thalassemia - Internet - Diagnosis - Therapy - Open access journals.

The dissemination and availability of up-to-date information on the research and achievements in the various field of human pathologies is a key-step to promote scientific collaboration between laboratories focusing on basic research, diagnosis and therapy on one hand, and involvement of associations of patients and on the other. In addition, being Internet available world-wide, the dissemination of scientifically-controlled data is necessary, when we consider the high interest of patients, families and low communities on the possibility to convert scientific research to therapy. In this specific case, the possibility of self-made therapeutic protocols is a clear drawback and should be limited by a strict control on the information made available on Internet. On this specific matter, interactive Networks involving all the researchers on hemoglobinopathies are attractive for presenting to the Internet users highly controlled information and the possibility of important interactions involving patients, clinicians and researchers. This review presents some examples of the information available on Internet concerning the research on thalassemia, including data about mutation analysis, therapeutic approaches, dissemination. Thalassemia is a genetic disease caused by low or absent production of globin chains (either α- or β-globin chains). The current therapy of thalassemia is based on blood transfusion and, when possible, bone marrow transplantation. However, therapeutic trials using inducers of fetal hemoglobin and employing gene therapy are under consideration.[1-5]

The Internet resources on β-thalassemia mutations

One of the best up-to-date data bank collection for β-thalassemia mutations is the one present on the

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globin gene server HbVar,[6] published by Hardison *et al*. on Human Mutation in 2002 [7] and further developed by Patrinos *et al*. in Nucleic Acids Research, 2004.[8] HbVar is a relational database of information about hemoglobin variants and mutations that cause thalassemia. HbVar results from a collaboration among several investigators at Penn State University (USA), INSERM Creteil (France), and Boston University Medical Center (USA). The initial data came from Syllabi, authored by Prof. THJ Huisman, Mrs. Marianne FH Carver, Dr. Erol Baysal, and Prof. Georgi D. Efremov. This information was converted to a database, and now new entries are added and old entries are corrected by curators from several institutions, including Dr. Henri Wajcman, Dr. George Patrinos and Dr. Nick Anagnou. The HbVar Database contains more than 1 000 entries of human hemoglobin variants and thalassemia mutations for population and sequence variation studies. In addition to HbVar, other data bank collection which update on thalassemia mutations can be found at the following links: beta.sproutcasa [9] (a site containing a beta-thalassemia mutation map), and at the link of Online Mendelian Inheritance in Man (OMIM, Johns Hopskins University),[10] The Human Gene Mutation Database (HGMD at the Institute of Medical Genetics in Cardiff,[11] of the "Syllabus of thalassemia mutations" (a compendium of the more than 300 thalassemia alleles and HPFH determinants developed by Titus HJ Huisman, Marianne FH Carver, and Erol Baysal).[12] A partial list of Internet resources available on thalassemia mutations is shown in Table I.

Several scientific journals were interested in the publication of novel gene mutations causing thalassemia. At the moment, among the scientific journals focusing on hemoglobinopathies, Hemoglobin is a reliable one.[13] The publications of hemoglobin variants or simply novel Hb-related mutations without impact on general concept in molecular and cellular biology are on the contrary discouraged in other well positioned journals, including Blood,[14] Human Mutation,[15] European Journal of Haematology.[16]

TABLE I.—*WEB sites on thalassemia mutations.*

Database	Link
HbVar	http://globin.cse.psu.edu/globin/hbvar/menu.html
OMIM	http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=141900
HGMD	http://www.hgmd.cf.ac.uk/ac/gene.php?gene=HBB
Syllabus on Thalassemia	http://globin.cse.psu.edu/html/huisman/thals/

The Internet resources on the development of therapeutic approaches

The Internet resources useful to obtain information on research aimed at the development of novel therapeutic approaches are clearly more heterogeneous, due to the different strategies followed by different laboratories for finding curative protocols for thalassemias. For instance, the web site "thalassemia on-line" [17] provides information, easily accessible and easy to read, of wide interest on thalassemia including cause, symptoms, diagnosis, and treatment. In addition, this site provides a list of world wide thalassemia associations and links. The web site of the "Cooley' anaemia foundation" [18] was developed by one of the most important American nonprofit health organisations and offers exceptional information on thalassemia. This site is of particular interest, especially for patients and their relatives. The easy to navigate web site of the "Children's Hospital Oakland-Northern California comprehensive Thalassemia Center" [19] includes comprehensive thalassemia information covering all aspects of care, from medical treatment to psychosocial issues. Answers to frequently asked questions are provided (of interest is also the "patient forum"). The Harvard Medical School and Brigham Women's hospital offer an overview on all aspects of Thalassemia and sickle cell disease as well as information on clinical management and research.[20] Finally, a very interesting site is the one produced by the United Kingdom Thalassaemia Society.[21] The society's aim is to provide relief and counselling to sufferers and carriers, to educate people on the problems associated with Thalassaemia and to bring together patients and families in order to exchange ideas and information. In the site a section on personal experiences and a book list of recommended reads and videos are also available.

With respect to thalassemia treatment, several links are present in the WEB describing the state of the art of the research in the fields of 1) bone marrow transplantation; 2) gene therapy; 3) stem-cell based therapies and 4) induction of fetal hemoglobin. Examples

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TABLE II.—*WEB sites for dissemination of information on Thalassemia.*

Thalassaemia International Federation	www.thalassaemia.org.cy
UK Thalassaemia Society	www.ukts.org
Thalassaemia Pakistan	www.thalassaemia.org.pk
Cooley's Anemia Foundation	www.thalassemia.org
Thalassaemia Foundation of Canada	www.thalassemia.ca
Children's Thalassaemia Foundation of Hong Kong	www.thalassaemia.org.hk
Northern Cyprus Thalassaemia Society	www.kibristalasemia.org
Fondazione Italiana "Leonardo Giambrone"	www.fondazionegiambrone.it
Thalassaemia Association of Malaysia	www.tam.org.my
Emirates Thalassaemia Society	www.thalassemia.org.ae
Thalassaemia Society (Singapore)	www.thalsociety.org
Thalassaemia Society of Victoria	www.tsv.org.au
Associacao Brasiliera dos Talassemicos	www.abrasta.org.br
The Chronic Care Centre -Lebanon	www.chroniccare.org.lb
Thalassaemics India – New Dehli - India	www.thalassemicsindia.org
Thalassaemia Association of Argentina 'Fundatal'	www.fundatal.org.ar
Taiwan Thalassaemia Association (TTA)	www.tta.org.tw
Thalassaemia Federation of Turkey	www.talasemi.org
National Thalassaemia Welfare Society - India	www.thalassemiaindia.org
Oscar Nederland -Netherlands	www.thalassemie.nl
Thalassaemia Foundation of Thailand	www.thalassemia.or.th
The Bangladesh Thalassaemia Foundation	www.thals.org
Ninava Thalassaemia Society	www.ninavasemia.blogspot.com
Associazone Veneta Per La Lotta Alla Talassemia (AVLT)	www.avlt.it
Berloni Foundation	www.fondazioneberloni.it
Thalforum	www.thalforum.com
Northern California Comprehensive Thalassemia Center	www.thalassemia.com
Egyptian Thalassemia Associatio	www.thalass-eg.com english info

of these sites, addressing specific issues in the field of current as well as developing therapeutic strategies are listed in Table II. The sites describing the research areas of the Italian groups are available at Thal Lab's site and the Cyprus Institute of Neurology and Genetics' site.[22, 23] A forum for patients and families can be contacted at Thalforum (Thalassemia Community Forum).[24]

The ITHANET project

FP6 founded several projects within the e-Infrastructure program, including Ithanet (Electronic Infrastructure for Thalassemia Research Network).[25] As clearly stated in the Ithanet portal, the major objective of this project is to enhance the scientific potential of the haemoglobinopathies' research community using infrastructures and tools of European research networks. Ithanet aims to harmonize and develop e-infrastructures for the coordination of existing research activities as a base for future collaborative projects. Using *e*Infrastructure tools to consolidate and strengthen a research community with a specific geographic distribution and research topic, Ithanet strives to create new opportunities for high impact collaborative research in the European Research Area. The Ithanet consortium comprises all of the major European research institutions active in the field and a number of collaborating partner institutions from non-EU Mediterranean and Black-Sea countries (Figure 1). In total, Ithanet associates 26 partners from 16 countries. In order to set-up and maintain interaction between the partners involved, as well as to coordinate training and project management activities, Ithanet utilizes teleconferencing technology. Additionally, Ithanet introduced media broadcasting and streaming technologies for conferences and teaching courses on haemoglobinopathies, contributing to the exchange and dissemination of good practices in the field of e-learning. Aiming to encourage a high level of interaction among members of the haemoglobinopathy community, a dedicated portal has been created.[26] Visitors to the Ithanet portal can quickly exchange information, share ideas, enhance the global awareness of

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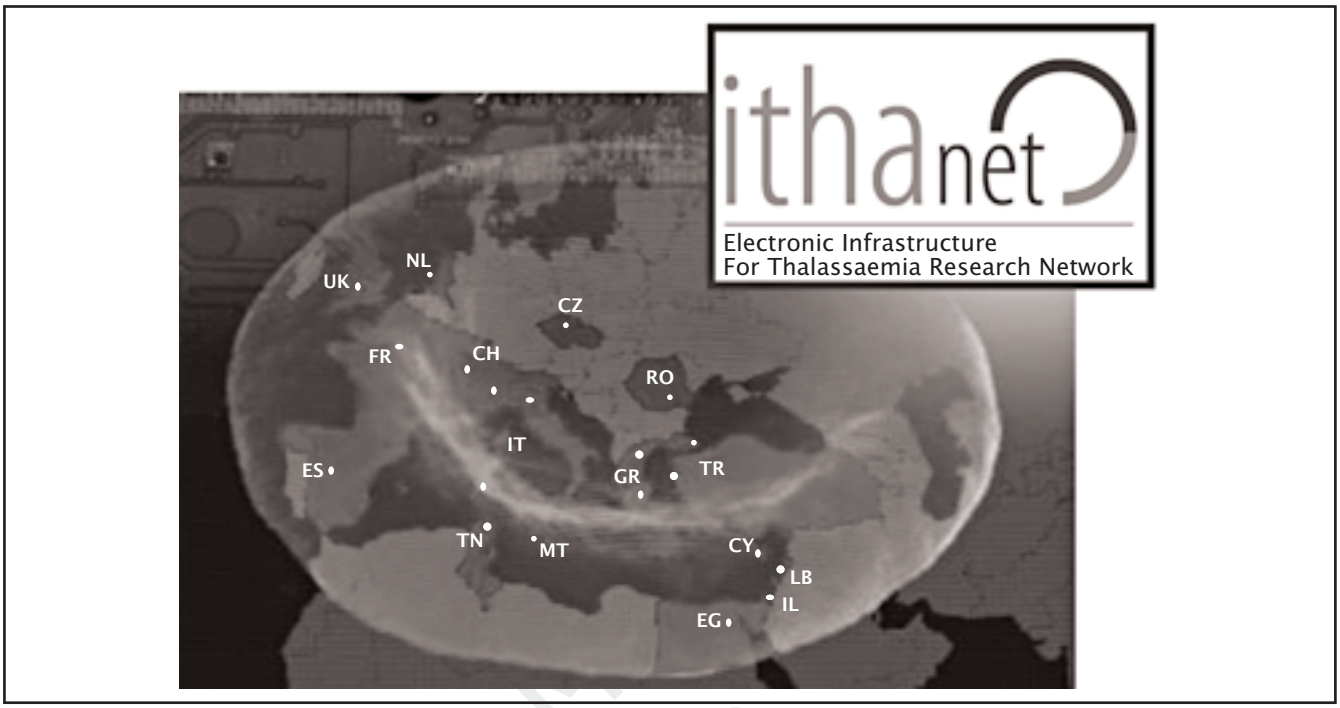

Figure 1.—Ithanet. Electronic Infrastructure for Thalassaemia Research Network.

pertinent issues, and help define critical areas of haemoglobinopathy treatment and research. The portal offers the latest news, techniques and information on haemoglobinopathies and also serves as a platform for the easy exchange of information and dialogues between interested groups, both patients and researchers. The portal is also used as a database of standard scientific protocols, methodologies, and repositories. It contains information on almost all Thalassaemia-related institutions and medical centres as well as patients and scientific societies. The list of the participants to the Ithanet project is included in Table III.

The role of the Thalassemia International Federation

The Thalassemia International Federation (TIF) [26] was founded in 1986 and is a key non-profit, non-governmental patient-driven organization. The very important mission of TIF is to achieve "equal access to quality healthcare for every patient with Thalassaemia across the world". To reach the objectives of the mission, TIF has been working officially with the World Health Organization since 1996. In detail, the major areas of activity of TIF are to 1) promote awareness and support studies about thalassaemia, including prevention, medical and other care; 2) disseminate the knowledge, experience and expertise gained from countries with successful control programmes to the needs in thalassemia research; 3) procure the right of every patient for equal access to quality medical care. As indicated in the TIF web site, these goals are expected to be achieved by several actions, including the establishment of new and the promotion of existing National Patient Associations, the organization of delegation visits to affected countries and the development of a network of collaboration with National, European and international organizations. The TIF magazine is a quarterly publication, containing news and information from its members around the world and the latest scientific and medical advancements in the field of haemoglobinopathies. Each issue is distributed to more than 4 000 subscribers in over 60 countries and 50 issues published to date. TIF is a partner of the Ithanet network.

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TABLE III.—*The participants to the Ithanet network.*

Partner		Organization	Country	Lead Researcher
P01	CING	The Cyprus Institute of Neurology and Genetics	Cyprus	Dr. Marina Kleanthous
P02	CESNET	CESNET, z.s.p.o.	Czech Republic	Dr. Eva Hladka
P03	TIF	Thalassaemia International Federation	Cyprus	Dr. Androulla Eleftheriou
P04	EGF	European Genetics Foundation	Italy	Prof. Giovanni Romeo, MD
P05	ORH Trust	Oxford Radcliffe Hospitals NHS Trust	United Kingdom	Dr. John Old
P06	UNICA	University of Cagliari	Italy	Dr. Galanello Renzo
P07	UoM	University of Malta	Malta	Prof. Alex Felice
P08	AG	Asclepion Genetics Sàrl	Switzerland	Dr. George Patrinos
P09	NKUA	National & Kapodistrian University of Athens	Greece	Prof. Emmanuel Kannavakis
P10	HMO	Hadassah Medical Organization	Israel	Prof. Eitan Fibach
P11	Uni Ferrara	Ferrara University	Italy	Prof. Roberto Gambari
P12	Min. of Health	Ministry of Health	Cyprus	Dr. Soteroula Christou
P13	Laikon GH	Laikon General Hospital	Greece	Dr. Ersi Voskaridou
P14	Cairo Univ	Cairo University	Egypt	Prof. Amal El-Beshlawy
P15	CCC	The Chronic Care Center	Lebanon	Prof. Ali Taher
P16	IRCCS S. Matteo	IRCCS Policlinico San Matteo	Italy	Prof. Franco Locatelli
P17	MI-EMC	Erasmus University Medical Center	Netherlands	Prof. Frank Grosveld
P18	LUMC	Leiden University Medical Center	Netherlands	Dr. Piero C. Giordano
P19	AHEPA UGHT	University General Hospital AHEPA	Greece	Dr. Helen Hasapopoulou
P20	IGUB	University of Bucharest	Romania	Prof. Lucian Gavrila
P21	Bo aziçi Univ.	Bo aziçi University	Turkey	Prof. Dr. A. Nazli Basak, PhD
P22	HET	Hopital d'enfants	Tunisia	Prof. Slaheddine Fattoum MD
P23	EUH	EGE University	Turkey	Prof. Yesim Aydinok
P24	INSERM	Institut National de la Sante et de la Recherche Medicale	France	Dr. Henri Wajcman
P25	FHCSC	Fundacion para la investigation biomedica del Hospital universitario clinico San Carlos	Spain	Prof. Ana Villegas
P26	GRNET	National Research and Education Network of Greece	Greece	Anastasios Zafeiropoulos

This table was taken from http://www.ithanet.eu.

From the laboratory research to the WEB dissemination: scientific journals interested in the online dissemination and open-access knowledge

The online dissemination of the publications concerning thalassemia is carried on by most of the leading journals in hematology, such as Blood, British Journal of Haematology, American Journal of Haematology, European Journal of Haematology. However, in most cases, the access to these journals is not open. Open access is guaranteed by other key scientific journals, such as Nucleic Acids Research and Journal of Clinical Investigation.

As far as the online dissemination through Open Access Journals (OAJ), it is very important first to define OAJ as journals that use a funding model that does not charge readers or their institutions for access and the use of the data published. It is very important to underline that users are freely allowed to "read, down-

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load, copy, distribute, print, search, or link to the full texts of these articles". This is mandatory for a journal to be included in the directories of OAJ.[28] Of course, the journals must activate peer-review process and editorial quality control to be included. An example of OAJ which has recently published articles on thalassemia is Evidence Complementary Alternative Medicine (e-CAM).[29, 30] A detailed list of open access journals can be found at the Directory of OAJ. This service covers free, full text, quality controlled scientific and scholarly journals. The final aim is to cover all subjects and languages. Currently the directory include 3 203 journals. At present 1 032 journals are searchable at article level. As of today 174 246 articles are included in the DOAJ service. Among OAJ considering the dissemination of studies on thalassemia and related pathologies, it is worth citing BMC Clinical Pharmacology, BMC Pharmacology, Drug Target Insights, PLoS Medicine, The Scientific World Journal, Journal of Automated Methods and Management in Chemistry.

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