Cystic Fibrosis European Network

NEWSLETTER

OCTOBER 2000 – N° 3

CONTENTS

NEWSLETTER CONTRIBUTIONS

The closing date for the next issue of the CF Thematic Network newsletter is December 31, 2000.
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EDITORIAL

Dear colleagues and friends,

The year is moving along very rapidly. The Thematic Network, however, is not planning to start its winter sleep. You will read in this issue of the newsletter that the QA for the laboratories has attracted close to 200 labs. The recommendations for CF testing have finally come off the prints of the Nature Group, as supplement to the European Journal of Human Genetics. Our experience with these QAs has even drawn the attention of the FDA in the US. Our network is being cited as one of the most successful undertakings in Human Genetics in Europe. So, do we rest on our wreath of laurels, or do we go ahead with this adventure?

I guess we owe it to the patients and their families to continue to structure and improve the CF services and research in Europe. Representatives from industry have shown a keen interest in the meeting planned in November. Let us hope that this will be the start of a fruitful collaboration. The different new subprojects are taking shape and will produce tangible results from next year on.

We will hear soon at the Budapest meeting from our friends in eastern and central Europe what we can do to help them in their, sometimes very difficult, working conditions.

So keep up the good work; contact us if you have an idea or a suggestion, a comment or a constructive criticism and ask Saint Nicholas all those equipments you would need to make your life and that of your collaborators easier.

Jean-Jacques Cassiman
Coordinator of the CF-network
Leuven, October 2000.

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ETHICAL, LEGAL AND SOCIAL IMPACT OF THE USE OF NEW DIAGNOSTICS AND THERAPEU-TICS

On October 2, 2000 Ingrid Dreesen has started as a research assistant at the Center for biomedical ethics and law at the K.U.Leuven. She graduated in July as master of law at the same University after following the course in medical law and making a scription on the protection of patients rights. All over Europe, patients rights is a rapidly evolving theme through legislation and jurisdiction. The 1997 Convention on Human Rights and Biomedicine of the Council of Europe has provoked in many member states of the European Union an intensified activity in this field. It is for this reason no surprise that I. Dreesen has started her research with this Convention. This Convention contains two dispositions that are of particular interest for the Thematic Network, articles 11 (prohibition of any form of discrimination on the ground of genetic heritage) and 12 (predictive genetic testing only for health purposes or for scientific purposes linked to health purposes and subject to appropriate genetic counselling). However, a clear understanding of these dispositions requires that they are placed within the general framework of the said Convention and the protection of human rights in health care in general. Moreover, the drafting of guidelines for the application of new diagnostics and therapeutics requires that the incorporation of the Convention into national law is clearly understood. Therefore, I. Dreesen will in a second phase of her research make a comparative analysis of the basic principles of patient's rights (consent, information, protection of privacy of medical data) in the different Member states of the European Union. Without such a broad understanding of patients' rights in general, every effort to draft guidelines in the field of the rights of patients afflicted by a genetic disease or carriers of such a disease will be futile. Patients' rights in Europe is also the theme of the inaugural speech of Herman Nys on the occasion of his nomination as professor in international health law at the University of Maastricht on December 1, 2000. The title of the speech is: Europatient: Towards a European Medical Services Law. Parallel with this broad study on patients' rights, I. Dreesen will under the scientific guidance of Kris Dierickx start collecting and studying relevant literature on ethical-legal issues related to genetics, insurance and employment.

Herman Nys, Leuven, Belgium

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WHAT IS HAPPENING UNDER THE CF NETWORK FOR THE DIAGNOSTIC MOLECU-LAR GENETIC LABORATORIES

At present the **quality assessment scheme 2000 for CF** is running. 195 laboratories received the samples in September. When all of them will return their genotype results, the raw data and the written reports to the scheme organiser, there will be 22 laboratories more than last year. The laboratories are dispersed over 24 different countries in Europe (Austria, Belgium, Cyprus, Czech Republic, France, Germany, Hungary, Italy, Latvia, Lithuania, Northern Ireland, Norway, Poland, Portugal, Republic of Macedonia, Russia, Slovak Republic, Spain, Sweden, Switzerland, The Netherlands, Turkey, U.K., Ukraine, Yugoslavia), in addition two laboratories from US and two from Australia participate.
In the newsletter of January we will announce the genotype results for the six samples. The final evaluation is foreseen for the end of March. As last year all the laboratories without genotype mistakes will receive a certificate of successful participation. More information on the quality assessment scheme for CF can be found on the website of the CF network (http://
www.med.kuleuven.ac.be/cme/cf/genetic_diagnostic_labs.htm
).

Recommendation for quality improvement of genetic testing in cystic fibrosis were published as a supplement of the European Journal of Human Genetics (September 2000). These recommendations were formulated by the steering committee of the previous European concerted action for CF (1996 - 2000). The supplement was distributed to 211 laboratories, registrated with their coordinates in our mailing list.

The recommendations provide general guidelines for the molecular genetic testing of cystic fibrosis in patients / individuals, general strategies for testing as well as guidelines for laboratories procedures, internal and external quality assurance, and for reporting the results, including the requirements of minimal services in mutation testing, the nomenclature for describing mutations, procedures to control false-positive amplification reactions and to validate tests, and guidelines to implement a quality system in a molecular diagnostic laboratory are reviewed.

In a nutshell the following recommendations were formulated:

- develop a quality system leading to accreditation by national or European agencies
- participate regularly in external QA trials

- test for different CFTR mutations up to a detection rate of at least 80% in the ethnic population of the individual
- use validated testing methods
- watch over the indications for CF testing by interacting with the involved clinicians
- provide relevant information to the clinical staff for appropriate risk calculation and counselling of the families
- create a network with other CF laboratories at regional, national, or European level to provide high quality level CF testing

We have the opportunity with the CF network to organise and bring people together for **workshops and training sessions**. A ***workshop on risk calculation*** is already planned, on Wednesday 16 May 2001 in Vienna, during the 10th International congress of Human genetics in Vienna. J. Ott (US) and C. Chapmann (UK) already confirmed to give lectures. You are all welcome.
Suggestions about topics to be covered in training sessions or workshops can be e-mailed to CF.network@med.kuleuven.ac.be.

Els Dequeker, Leuven, Belgium

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ADVANCES IN THE ACTIVITIES OF THE WORKING GROUP ON CFTR EXPRESSION - RESOURCES

The Working Group (WG) on CFTR Expression – Resources counts now with 48 members. Membership is totally free and open to any scientist in the CF field. Members receive the Newsletters on CFTR Expression (see below) besides additional information and news from the CFTR Expression WG. To apply for membership please consult the CFTR Expression webpage (see below).

The webpage of the CFTR Expression WG, although still under construction (between Lisboa and Leuven) already exists as a sub-webpage of the CF Network and soon will be complete for further information on the activities of the WG.
(http://www.med.kuleuven.ac.be/cme/cf/CFTRExpression.htm)

One of the specific aims of the WG is the creation of a virtual catalogue of methods and resources (i.e., a 'Virtual Repository') to be used freely by the scientific community as a tool for the study of CFTR expression. Based in a great extent on the existing similar catalogue from the AFLM (whose help, in the person of Stephane Mazur we acknowledge) the structure of this Virtual Repository already exists in a draft version. This version has been published in the 2nd issue of the Newsletter on CFTR Expression (September issue) and has been sent to all members of the WG to receive comments and suggestions for improvement. It is expected to be soon on-line as well (at the moment only available on-line through Newsletter no.2). All scientists working in the field of Cystic Fibrosis are encouraged to contribute to this Virtual Repository (for details, please consult our webpage).

The Newsletters on CFTR Expression are available on our webpage (see above) and contain reports on the six methodological expertise areas of the WG (namely: transcript analysis; cell biology and histology; protein biochemistry; cell physiology; in vivo and ex vivo functional assessment; and models).

The next annual meeting of our WG will take place in Estoril (near Lisbon) between 30 March and 1 April, 2001. Deadline for abstracts and registration: 28 February 2001. The meeting will be open to all scientists in the CF field who are interested in discussing and reporting CFTR expression with a focus on methodological approaches. Funds are available to cover travel, and/or registration + accommodation expenses for a limited number of participants. Therefore, contributors to the Virtual Repository will be given preference in the distribution of these funds.

The CFTR Expression WG also promotes the exchange of scientists between labs for the acquisition or comparison of methodologies used in CFTR expression studies, by covering travel and accommodation costs (up to 750 Euro). From each visit a contribution to the Virtual Repository is expected (en entry such as a novel cell line, a new antibody, etc. or a protocol), besides a small report to be published in the CFTR Expression Newsletter. Anyone interested in applying to visit another lab for this purpose should consult our webpage (see under: 'Applying for Training and Travel Grants'). The first of these visits already took place in September.

Margarida D. Amaral, Lisboa, Portugal
Sebastian Beck, Lisboa, Portugal

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A SHORT HISTORY OF HOW THE INFORMED CONSENT RECITAL CAME INTO THE EU BIOTECHNOLOGY DIRECTIVE

It took the European institutions a decade to agree on the Biotechnology Directive, because they differed greatly with regard to the ethical considerations that should be incorporated. The Commission and the Council (the latter representing the governments of the different Member States) originally considered it to be inappropriate for patent law to deal expressively with those ethical considerations, while the European Parliament held the opposite view. This stand-off continued for over ten years.

Only gradually the Commission and the Council gave in and agreed with the substance of many of Parliament's ethical amendments. The latter however, had vastly increased over time. Parliament's more recent ethical concerns resulted either from recent biotechnological developments such as the use and or cloning of human embryos, or from developments in international law (the signing of new international treaties), which had to be complied with.

The informed consent requirement is an example of the latter. It only came into the spotlights two months before the Committee of Ministers of the Council of Europe adopted the Convention on Human Rights and Biomedicine in November 1996. Article 22 of that Convention contains an informed consent requirement. (See article in first newsletter.)

The European Parliament then proposed to make the informed consent requirement legally binding in patent law: no patent would be granted if this requirement was not met (amendment 76 proposing a new article 8 bis §2). In order to prove that this requirement was met, patent applicants would have to disclose in their applications inter alia the donor's name and address. The European Commission rejected this amendment with the convenient argument that this would violate the donor's privacy.

This raises the question whether the Commission did not overreact: is there really no way of reconciling informed consent and privacy in patent law?

The Belgian governmental delegation tried to salvage informed consent. It proposed to incorporate it in the Directive not as a technical requirement (as Parliament did), but as an ethical requirement, which would be worded as being of Public Order and Morality. Eventually this proposal did not make it either and the informed consent requirement was only mentioned in the recitals. Contrary to the articles in the Directive, recitals are not legally enforceable.

Although the Belgian government did not succeed in having its proposal adopted, it still intends to implement the Directive with the informed consent requirement as an additional example of the *Belgian* Public Order and Morality. (The latest draft proposal does not differ substantially from the one mentioned in the first newsletter.)

The Directive should already have been implemented into national law (the deadline for implementation was July 31, 2000). As far as we know, Finland, Sweden and the UK are until now the only Member States to have implemented the Directive. This seems proof of how ethical considerations (about informed consent or about other topics) continue to haunt the EU Biotechnology Directive. This makes them so interesting to study.

To be continued…

Pierre Saelen, Leuven, Belgium
Geertrui Van Overwalle, Leuven, Belgium

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ANNOUNCEMENTS

Meeting with the Industry - Brussels, 28 November 2000

To activate the industry partnership relations in the CF network, we invited representatives from a series of companies for a round table discussion on the following topics: what is the CF Thematic network and what could be the involvement of industrial partners in the network. The following companies confirmed their attendance: Applied Biosystems, Bayer, Ingeny, Innogenetics and Roche.

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Workshop Risk Calculation

During the 10th International congress of Human genetics in Vienna, the European CF network will organise a workshop on Risk Calculation. J. Ott (US) and C. Chapmann (UK) already confirmed to give lectures. You are all welcome

Conference website: http://www.ichj2001.org

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European CF Network International Symposium 2000 for Eastern and Central Europe
Budapest, Hungary, 2-3 December 2000.

Saturday, December 2, 2000.

Arrival to Budapest
14:00 - 16:00 Scientific program I. Session
16:00 - 16:30 Tea break
16:30 - 18:00 Scientific program II. Session / Poster presentation
19:00 - 22:00 Welcome Party - Dinner and Hungarian folklore show
("Udvarhaz" Restaurant)

Sunday, December 3, 2000.

08:00 - 09:00 Breakfast in the Hotel
09:30 - 11:00 Scientific program III. Session / Poster presentation
11:00 - 11:30 Coffee break
11:30 - 13:00 Scientific program IV. Session
13:00 - 14:00 Lunch
Free afternoon

The following speakers already confirmed their attendance and will give a presentation:

- B Tümmler (Germany) European Cystic Fibrosis Twin and Sibling Study: Clinical epidemiology, basic defect and genetic modifiers
- C De Boeck (Belgium) Burkolderia cepacia: a Belgian prevalence study
- C. Bombieri (Italy) CFTR related diseases
- E. Dequeker (Belgium) Genetic proficiency testing in diagnostic laboratories: quality is the message
- G. Miklos (Hungary) The Hungarian Cystic Fibrosis Database I: Statistical analysis and clinical data
- G. Fekete (Hungary) The Hungarian cystic Fibrosis database II: Genetic information

Selected abstracts for oral presentation and the final program will be available on the website after November 15, 2000.

(http://www.med.kuleuven.ac.be/cme/cf/meetings.htm)

If you would like to participate, please contact

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or the local organiser:

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Steering committee meeting

The second **steering committee meeting** of the CF network will take place in Verona, January 27-28, 2001

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Manual for CF patients and family

As indicated in the Newsletter of July, a manual for CF patient and their family is available in English, French, German, Italian and Spanish. The manual includes the following topics:

- what is cystic fibrosis
- what happens in the lungs
- what happens in the pancreas
- when to suspect cystic fibrosis
- how is cystic fibrosis inherited from the parents
- to have a child with CF … and to accept a child with CF
- treatment of cystic fibrosis
- hospital
- relatives and friends
- you are not alone

The manual was sent to different CF associations. If you are interested to receive these manuals please contact the coordination center of the CF network (E. Dequeker) or e-mail to CF.network@med.kuleuven.ac.be

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Blood samples of CF patients and carriers

In the newsletter of July 2000 there was a call for blood samples of CF patients and carriers. Many thanks to those who responded. Unfortunately the preparation of the general informed consent has taken more time. In the next newsletter we will come back on this issue.

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CFTR-gene primers for DGGE

Ingeny International offers a special price for the CF network members ordering CFTR-gene primers for DGGE. For more information see Newsletter July 2000 or contact:

Ingeny International BV
Amundsenweg 71,4462 GP Goes
The Netherlands

Tel. +31 222 920 - Fax +31 222 923
http://www.ingeny.com - e-mail: info@ingeny.com

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CONGRESSES AND MEETINGS

Under this heading we would like to inform you on congresses and meetings of interest to members of our CF network. If you organise a meeting open for public, please inform us. We will be happy to announce via the CF network newsletter and website. Please inform us also about other interesting meetings not yet mentioned in this list.

North American CF congress Baltimore, Maryland, U.S., 9-12 November 2000.
Conference website: http://nacfc.cjp.com
or e-mail at NACFC@cff.org

ICHG congress
International congress of Human Genetics,
Vienna, Austria, 15-19 May 2001
Conference website: http://www.ichj2001.org
Abstract receipt deadline: December 15, 2000
CF-network: Wednesday May 16, Workshop on Risk Calculation

24th European Cystic Fibrosis Conference
Vienna, Austria, 6-9 June 2001
Conference website: http://www.ecfsoc.org/
or e-mail at congress@mondial.at
Abstract receipt deadline: March 1, 2001
Parallel session of the CF-network

4th Australian Cystic Fibrosis Conference
Brisbane Queensland, Australia, 23-25 August 2001
Conference office: Cystic Fibrosis Australia,
PO Box 254, North Ryde NSW 1670, Australia
or e-mail: general@cysticfibrosisaustralia.org.au

ASHG meeting San Diego, California, U.S. 12-16 October 2001.
Conference website:
http://www.faseb.org/genetics/ashg/ann-meet/ashgmeet.htm

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