Cystic Fibrosis European Network

NEWSLETTER

NOVEMBER - DECEMBER 2003 – N° 12

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NEWSLETTER CONTRIBUTIONS

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EDIOTRIAL

Dear friends and colleagues,

The official activities of the EC funded CF Thematic Network are gradually coming to an end. Indeed, the funding of the network will officially end on January 31, 2004.
More than 12 years of support by the EC for the CF diagnostic activities in Europe, through various Biomed, FP4 and FP5 projects, is irrevocably ending in this way. It is a rather sad moment after so many years of continuous efforts by so many participants to improve and structure our services for the patients and their families.
But rather than getting depressed and to lament for hours, lets look at what was realized and what we can do in the future.
We can all be very proud. The subtitle of the thematic network was 'Cystic Fibrosis as a model disease for other genetic diseases'. I am sure that we have contributed substantially to being this model. The output of the Network (see our website) has been exceptional over the years. There are deliverables important for science, for the diagnostic services but also for the patient and parent support groups. There have been activities in the EU, in the NAS countries but also in Eastern Europe and on other continents. The CF Thematic network and its participants are well known all over Europe and beyond.
Time therefore to thank all of you for your continued interest and contributions. A special thanks to Els Dequeker and Claudia Vits for all the work done to improve the quality of the diagnostic services, to Margarida Amaral and her collaborators for collecting all these wonderful resources, to Herman Nys and collaborators for his contributions on informed consent and patient rights and to all the other Steering committee members for their contributions and support.
I am sure that some of the activities of the network can be continued by the ECFS. It is also clear now that the EQAs for the diagnostic labs will, at least for 2004, continue with the financial support of diagnostic companies. Moreover, there is still a chance that the EC will put CF back on the list of topics of the 6th FP and that a new network can be put together in the coming years.
Who knows what else the future might bring.
No reason therefore to get depressed. All the more reason to continue to work on improving our services to the patients and the families and to stay in contact with each other.

It was a pleasure and an honor to serve you all during these years. Lets build on the achievements of the past.

Jean-Jacques Cassiman
Coordinator of the CF-network
Leuven, November 2003

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7th INTERNATIONAL SYMPOSIUM FOR CYSTIC FIBROSIS
BRATISLAVA, SLOVAKIA, SEPTEMBER 20, 2003

The 7th International Symposium for Cystic Fibrosis, and sadly probably the last one, organized within frames of the Thematic Network on CF, was held on September 20th, 2003, in Bratislava, capital of Slovak Republic. 76 participants (the greatest number in the last few years) representing 14 different countries attended the meeting actively. This great number of participants witnesses the traditionally high scientific standard of these meetings, which represented an outstanding p.

Also in Bratislava gave presentations well recognized invited international experts on specific topics of importance from molecular genetics to clinical management, as M. Macek and V. Vavrova from Prague, H. Cuppens from Leuven, P. Vandamme from Gent, and C. Sevens from Brussels. In addition, the participants had the opportunity to share and discuss their own experience in the management of CF through an oral or a poster presentation. Altogether, 28 talks and 13 posters were presented. The topics of the presentations varied from the patients care in the different countries, over approaches in confirming the diagnosis, difficulties in DNA testing, the scale and frequency of mutations, management of CF centres, identification of *Burcholderia cepacia* complex, genotype – phenotype correlations, and the role of physiotherapy in CF. During the coffee breaks the 13 posters were actively viewed and discussed. After this rich and exhausting program the meeting was closed by a well-deserved dinner.

The participants left Bratislava with a hope that, the activity of the Thematic Network on CF will be renewed, and in its frames the tradition of these useful meetings will continue in succeeding years.

Ludovit Kadasi, Bratislava, Slovakia

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WORKSHOP DIAGNOSTIC LABORATORIES FOR NORDIC / BALTIC COUNTRIES
LUND, SWEDEN, SEPTEMBER 11-12, 2003

The meeting gathered approximately 25 delegates, including 14 representatives from non-profit clinical genetic diagnostic laboratories (Finland, Sweden, Norway, Denmark, Lithuania, Estonia), 6 representatives from the industry (Nanogen/AH diagnostics, Innogenetics, Abbott, Orchid Biosciences), and 4 local (Swedish) physicians who meet CF-patients in their daily work or deal with obstetric aspects of the disease. Before the meeting, the local organiser provided the participating clinical laboratories with a questionnaire about their CF-related activities. The answers were reviewed and discussed during the meeting in an attempt to find similarities and differences between laboratory facilities. Presentations were held by each participating company during a separate industrial session. Non-commercial presentations during the meeting:

Review of questionnaire (see above)
Samuel Gebre-Medhin (Lund, Sweden)

CF-European network: Presentation of EQA data and best practice protocols
Els Dequeker (Leuven – Belgium)

CF- clinical aspects
Peter Meyer and Leena Mared (Lund, Sweden)

Ecogenic bowel syndrome in ultrasound as a prenatal marker for CF
Maria Westin (Malmö, Sweden)

Neonatal screening – status presens in Sweden)
Lena Hjälte (Stockholm, Sweden)

CF diagnostics: Experiences and approaches at the Copenhagen Centre (CANCELLED)
Marianne Schwartz (Copenhagen, Denmark)

What's next
Els Dequeker (Leuven – Belgium)

Samuel Gebre-Medhin, Lund, Sweden

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BENELUX WORKSHOP FOR DIAGNOSTIC LABORATORIES
LEUVEN, BELGIUM, OCTOBER 23-24, 2003

Quality Improvement for genetic testing – Cystic Fibrosis used as model disease

Present: Dorien Bex, Sebastien Boulanger, Kathleen Claes, Harry Cuppens, Katie De Pauw, Els Dequeker, Maria D'Hollander, Dennis Dooijes, Hans Gille, Patty Hendrix, Sabine Hermans, Pascale Hilbert, Henny H. Lemmink, Wil Loots, Gert Matthijs, Michael Morris, Gwenda Rabelink, Catherine Rydlewski, Ivo Salden, Hans Scheffer, Sara Seneca, Richard Sinke, Katrien Storm, Wolfgang Trautwein, Raoul Van de Graaf, Katrien Van den Bosch, Greta Van der Cruyssen, Marleen Van Honnacker, Crool Velter, Annemie Vergote, Katrien Verschueren, Katrien Weckx

This Benelux workshop was organised in Leuven, October 24th (and the evening of October 23rd). The main two topics were 'Testing and reporting of Cystic Fibrosis tests' and 'Quality Assurance in molecular genetic diagnostic labs'. One other primary objective of the workshop organisers was to facilitate personal contact between the different participants in an informal atmosphere. Besides representation from most Belgian and Dutch diagnostic laboratories, a number of companies in the field were also represented.

Most attendees arrived in the evening of October 23rd and after a welcome drink and a sumptuous meal, new contacts were made and old contacts and friendships were renewed.

On Friday, Els Dequeker started by evaluating the lessons learned by 7 years of CF QA-schemes. Over the years, the number of participating labs has grown from a few tens to almost 240 participating laboratories in the 2003 scheme. The overall conclusion is that quality (both of genotyping and of reporting) has steadily improved over the years. A remarkable recent observation is that labs handling larger volumes of samples make less mistakes than labs performing a small number of analyses per year.

Harry Cuppens discussed dHPLC and direct sequence analysis as two techniques which can be used to analyse the complete CFTR gene subsequent to standard analysis. dHPLC requires a lot of optimisation and decision making per patient to decide which fragments to analyse further by sequence analysis. Direct sequence analysis is suitable for automation, especially after development of multiplex amplification of all CFTR fragments in 6 PCR reactions, but (still) relatively expensive. Extensive discussion followed this presentation on when to use complete analysis of the complete CFTR gene in a diagnostic setting.

Hans Scheffer discussed the current situation for CF testing in the Netherlands. By law (art. 2 WBMV), in the Netherlands only DNA-diagnostic laboratories of departments of Clinical Genetics are allowed to perform test for monogenic disorders. CF testing in the Netherlands is performed by three of those laboratories, in Amsterdam, Groningen and Rotterdam. Lately, more and more laboratories from peripheral hospitals are starting to perform CF testing. In the coming years, the DNA-diagnostic laboratories will face the challenge to establish networks with these peripheral laboratories in order to organise responsibilities and ensure quality and patient well-being.

Discussing CF QA-scheme test results in workgroups closed the morning session.

In the afternoon, Els Dequeker and Gert Matthijs discussed the need for harmonisation in the process of QA and the strive for accreditation according to ISO standards, using the DDQA group as an example for validation of the dHPLC method.

Michael Morris, Hans Scheffer and Els Dequeker discussed their experiences, the common shortcomings and the pitfalls in setting up a quality assurance system in their respective labs. Validation of test methods and the importance of (good writing of) a good Quality Handbook were discussed.

After a farewell drink, everybody left to go to their respective homes with new insights.

Everybody? No, not everybody… in an ultimate attempt to demonstrate newly intensified collaboration, Els Dequeker and Hans Scheffer brought the author of this comment, whose exhaust-pipe dropped from under his car, to the local garage. In the end, the car was fixed and we all got home, exemplifying the success of this Benelux meeting.

D Dooijes, Rotterdam, The Netherlands

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EUROGENTEST …. WHAT IS THIS?

EUROGENTEST is a large collaborative proposal, a Network of Excellence, coordinated by Professor Jean-Jacques Cassiman (Leuven, Belgium) under the EU 6th Framework (FP6) that is being submitted in November 2003. The proposed network intends to develop the necessary infrastructure, tools, resources, guidelines and procedures that should lead to harmonization and improved overall quality of genetic services (cytogenetic, molecular, biochemical and clinical). This network will bring together experts and expert centers available across Europe on different aspects of genetic testing, including researchers, SMEs (small/medium sized enterprises), genetic testing laboratories, quality management and public health experts, ethicists, lawyers, sociologists and consumers.

To facilitate communication with all genetic centers in the EU, representatives of the European Society of Human Genetics (ESHG), ECA, and presidents of the National Human Genetics Societies have been included in the Advisory Board. The advisory board will act as a key sounding board to direct the program based on scientific, clinical and industrial expertise.

Jean-Jacques Cassiman will perform the overall coordination of the project with assistance from a deputy and operational management group. A Steering committee will be responsible for the operation and development of the project and will consist of Unit Leaders, their co-leaders and the coordinators of the project.

There are six Units within the Eurogentest network with Unit 1 as key unit of the Network. Each unit is subdivided into work groups and their respective work packages. The leaders of the units and coordinators of the work packages include representatives from most European countries. There are 25 work packages within the Eurogentest project. Each work package has a coordinator(s) and consists of objectives, description of the work, milestones and deliverables. The largest Unit, Quality management and accreditation/certification of genetic testing is led by Els Dequeker and Mike Morris and includes several work packages on accreditation of genetic testing and EQA of genetic tests. The different units are detailed below.

UNIT 1 ***Quality Management and accreditation/certification of genetic testing***
Els Dequeker (Belgium); Michael Morris (Switzerland)
Workgroup 1 - Consensus Procedures and guidelines on Quality Management and Quality Assurance (QA)
Workgroup 2 - Coordination of activities- database of QA information across Europe

Workgroup 3 – External Quality Assessment (EQA) schemes (Individual work packages for cytogenetics, molecular and biochemical genetics, including EMQN activities)
Workgroup 4 - Reference Measurement systems (measurement procedures and material).

UNIT 2 Information Sources and bio-informatics tools
S. Ayme (France); B. Dallapicola (Italy)

UNIT 3 Clinical Genetics, Community Genetics and Public Health
Ulf Kristoffersson (Sweden); Joerg Schmidtke (Germany); Helena Kääriäinen (Finland)
Workgroup 1 - Health Technology Assessment and Clinical Validation of Genetic Testing
Workgroup 2 - Quality Genetic Counseling

UNIT 4 Ethical, Legal, IPR and Social Issues
Herman Nys (Belgium); Jorge Sequieros (Portugal)
Workgroup 1 – Ethical Issues
Workgroup 2 - Legal Issues
Workgroup 3 – Public and Professional Policies Issues

UNIT 5 Research and Emerging Technologies
Bert Bakker (Netherlands); Andre Reis (Germany); Gert Matthijs (Belgium)

UNIT 6 Education
Alastair Kent (UK); Domenico Coviello (Italy)

The overall aims of the project are to:-
1/ Establish a network of quality across Europe
2/ Promote research, proper utilization, quality control and assurance and
adequate management of genetic services.
3/ To harmonize the accreditation and certification of genetic testing laboratories and the EQA schemes for Cytogenetics, biochemical and molecular genetics at a European, regional and national level throughout Europe.
4/ Establish procedures and guidelines for the validation of methods and technologies
5/ To identify present and future needs for Reference Measurement Procedures and Materials for genetic testing.
6/ Too provide genetic healthcare workers, the end-users and health care authorities with a portfolio of quality-assured information sources and informatic tools that are subject to validation and quality procedures.
7/ Improve the quality of genetic counseling services in connection with genetic testing in different European Countries.
8/ Prepare a directory of organizations that provide and produce educational material for the public. Institutional courses and education for genetic training (e.g. Masters degree) will be evaluated and criteria for quality defined.

More information about the Eurogentest will be published on the website www.eurogentest.org (In preparation) if the proposed project is funded. The evaluation of the project will be done in spring time.

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REPORT ON VISIT TO THE LABORATORY OF DR. DAVID N. SHEPPARD, DEPARTMENT OF PHYSIOLOGY, UNIVERSITY OF BRISTOL (BRISTOL, UK) FROM APRIL 28TH – MAY 23RD, 2003

The purpose of Alessandro Taddei's (AT's) visit to the Department of Physiology at the University of Bristol was to acquire skill in studies of wild-type and mutant CFTR Cl^- channels using excised inside-out membrane patches. Towards this goal, AT studied C127 and FRT cells expressing wild-type CFTR and the G551D mutant with Drs. Zhiwei Cai (ZC) and David N. Sheppard (DNS). ZC carefully taught AT how to design and execute studies of single channels and analyse the data. Following training, AT assisted ZC with a study of the single-channel properties of the G551D mutant. They discovered just how dead a channel G551D is with channel openings of reduced duration separated by closed periods lasting minutes! This presented a significant difficulty establishing the number of active channels per membrane patch. Thus, AT, ZC and DNS explored a variety of strategies including attempting to "lock" G551D channels open to establish accurately the number of channels per patch. Despite the altered gating behaviour of G551D channels, AT and ZC discovered that the fluorescein derivative phloxine B stimulated channel activity and that the mechanism of stimulation resembled that of the wild-type CFTR Cl^- channel. In summary, this visit was an excellent opportunity (i) to thoroughly equip AT for studies of the effects of CFTR modulators on wild-type and mutant CFTR Cl^- channels using excised inside-out membrane patches and (ii) for ZC and DNS to study with AT the single-channel activity of G551D.

Alessandro Taddei and Olga Zegarra-Moran, Genoa, Italy

Zhiwei Cai and David Sheppard, Bristol, UK

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ANNOUNCEMENTS

CF EXTERNAL QUALITY ASSESSMENT SCHEME 2003

242 laboratories (208 European laboratories from 30 countries, 33 labs of the USA, 1 lab of Australia) participate to the CF EQA scheme of 2003. 6 samples were sent to each participating laboratory in September 2003. Deadline for submitting data is December 15, 2003.

The evaluation of the results will be sent by June 2004 (foreseen). The correct genotypes of the QC samples will be sent at the end of January.

Els Dequeker, Leuven, Belgium

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MANUAL FOR CF PATIENTS AND FAMILY

Thanks to Innogenetics, Roche, Orchid, Abbott, Nanogen, Transgenomics for supporting one or more meetings (Bratislava, Lund, Leuven)

A manual for CF patients and family is available in English, French, German, Italian, Spanish, Czech and Slovak, Croatian, Ukrainian, Latvian, Serbian and Russian. Recently the manual has also been made available in Hungarian, Lithuanian, Polish and Macedonian. All languages can be downloaded as a pdf file from the CF network website (http://www.cfnetwork.be/Informationdocuments.htm)

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

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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 the CF network. If you organise a meeting open for the public, please inform us. We will be happy to announce your meeting via the CF network newsletter and website. Please inform us also about other interesting meetings not yet mentioned in this list.

4th Meeting with Industrial Partners
Brussels, Belgium, 27 November 2003
Contact:
Jean-Jacques.Cassiman@med.kuleuven.ac.be
Els.Dequeker@med.kuleuven.ac.be

Reporting & Interpretation of CF Test Reports
Leuven, Belgium, 28-29 November 2003
Contact:
Jean-Jacques.Cassiman@med.kuleuven.ac.be
Els.Dequeker@med.kuleuven.ac.be

ESHG meeting
Munich, QC workshop Monday, June 12-15, 2004
http://www.eshg.org/ehgc.htm

European CF Meeting Birmingham
June 11-15, 2004
http://www.cftrust.org.uk/cf2004/

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