# European Society of Human Genetics

# April 2005 / Newsletter No. 12

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# From the President of ESHG



Prof. Leena Peltonen

One year as a President of any Society passes so fast. After the great leadership of Veronica van Heyningen, it was a real challenge to take over this position. I think for years to come she will remain as a role model for ESHG Presidents with her charming efficiency.

I very quickly found out that the task of the President makes you very humble. You recognize that in a year you really can accomplish very little. You also recognize immediately that all the actual input and work is delivered by the secretary general and the critical subcommittees. Our secretary general, Helena Kääriäinen, conveniently also in Finland, has truly delivered whatever I did not know. She found the answers or accurate information, and whenever I stumbled in the details of the board meetings, Helena -seemingly effortlessly- helped me out.

I still find it amazing that although the chairs of our subcommittees obviously have their professional demands elsewhere, they all still want to contribute to the betterment of our society. They really show their academic citizenship on the European scale and we owe them tremendously. Especially I would like to emphasize the essential role of the scientific program committee. This committee operates truly professionally, the members provide their top level expertise and shamelessly utilize their personal links

with top geneticists world-wide to produce year after year a superb program for our main event: The annual meeting of ESHG.

The Munich meeting was a real success and my expectations for the Prague meeting are very high. The scientific program looks excellent and the local organizers under the leadership of Milan Macek have truly made an effort to arrange an unforgettable meeting for our membership in this beautiful European capital.

Perhaps the most critical position of our Society in this information era is held by the Editor of Chief of European Journal of Human Genetics, Gert-Jan van Ommen. It is solely thanks to his endless energy and continuing efforts that we have a European Journal that we all are so proud of.

Finally I would like to bring up one special act our society has greatly contributed, thanks to the efforts of Gert Matthijs. ESHG was this year one of the signing organizations to oppose the patenting of gene tests blocking free use of diagnostic DNA-tests. It is obvious that with gestures like this we can really influence the ways how genetic innovations will be used in the future in Europe and elsewhere.

Societies are like humans and consist of humans. They remain alive and well only if their members are dedicated to them and decide to share their dreams and passion for better tomorrow with their colleagues. The dreams and ambitions of our members fuel the operations of the Society. Our members want European genetics lead the way and become an essential element of our society. They want the huge amount of new genome-wide information to be translated to knowledge and understanding of biology and to better actions to heal and cure. We are living critical years. The genome project has provided us with accurate information of the genome anatomy of human and other species. Geneticists worldwide are facing a tremendous challenge how to wisely read and use this information. We cannot anymore excuse ourselves from really contributing to the betterment of mankind. Genetics is never more a marginal field of biology. Our research plans should be bold and ambitious, our desire to collaborate across funding agencies and research fields strong and our common will to build European resources and genetic platforms solid. We can accomplish a lot, especially since the European health care system provides us with the infrastructure facilitating not only unique research programs but also rapid translation of new genetic inventions to the improved health of our citizens. Our members recognize the challenge, they work to make their dreams to reality and our society should make every effort to help them to live their dreams. We should have good strategic links with the key players in the European Community, European Science Foundation and future European Research Council. We must learn to speak with one voice and take our responsibility to develop European research area. Staying connected with its members the European Society of Human Genetics can have a real impact on future of our continent, let's all work together to build and intensify those connections. For the next year Andres Metspalu will lead us towards this goal.

Leena Peltonen

## Secretary-General's Report



Prof. Helena Kääriäinen

The past year, from Munich to Prague, has again been both busy and successful for the Society. The details of what really has happened can be read in the activity reports in this Newsletter.

One of the biggest changes is that the administration of the membership has now been taken care of by Vienna Medical Academy. You may not have noticed the change as it went so smoothly. Karen Knob in VMA takes care of the daily contacts to and from the membership and Jerome Del Picchia collaborates with the committees, organizes most of the practical matters of the yearly conferences and takes care of a lot of other issues. Among other things, you may all have noticed the refreshing new looks and organization of the Society's homepage!

Our President, Leena Peltonen, as well as other members of the Executive Board have discussed on several plans for future activities for the Society; you will hear all about them in the membership meeting or, if you do not come to Prague, from the next Newsletter.

This was my first year as Secretary-General. It was interesting and enjoyable but I must confess, quite confusing as well. Fortunately the previous Secretary-General Peter Farndon has kindly replied to my numerous emails without delay.

I would love to get suggestions for the Board and other feedback from the membership. Send me emails or come to talk to me in Prague!

Professor Helena Kääriäinen

## Minutes of the European Society of Human Genetics Membership Meeting Munich, June 14th 2004

The meeting was opened by President of the Society, Veronica van Heyningen at 18.45

## 1) Activity Report 2003-2004 (Peter Farndon)

Complete reports of the committees' activities were published in the May Newsletter and Peter Farndon referred to them in his report. At the time of the year, it was not possible to know the final number of membership but the slight increase could be assumed to continue.

Gert-Jan van Ommen, Editor-in chief of EJHG, reported that the number of submissions to EJHG had been 40-50 / month and the acceptance rate 45%. The number of on-line readers had been steadily growing.

## 2. Financial Report of the Society 2003

The complete accounts of 2003 were presented and accepted.

### 3. Discharge of the Board Members for the year 2003-2004

The new President of the Society, Leena Peltonen, was not able to be present in the meeting and so Vice-President Veronica van Heyningen continued to chair the meeting. She was thanked by Peter Farndon for her year as President and welcomed as Vice-President. She thanked the retiring Board members Anne Hagemeijer-Hausman, Rodney Harris and Gerd Uterman. She also thanked Lisbeth Tranebjaerg, Deputy Secretary General, for her valuable work. Finally, very special thanks were given to Peter Farndon for his long and extremely valuable role as Secretary General.

### 4. Results of election for President-Elect and for Board Members

There was no election as the number of proposed candidates was just what was needed. Andres Metspalu was welcomed as President-Elect. Nurten Akarsu, Jacques Beckmann, Dian Donnai and Alessandra Renieri were welcomed as new Board Members. Andrew Read was welcomed as Treasurer, Helena Kääriäinen as Secretary General and Thomas Meitinger as Deputy Secretary General.

### 6. Membership fees 2005

It was decided that the membership fee will be increased only if that is necessary for NPG.

## 7. Sites of future European Human Genetics Conferences

The next conference will be in Prague. Site of the 2006 conference was not finally decided yet.

### 8. On-line membership record

There have been requests for an on-line membership record. Board had discussed it and suggested that a record should be started. This suggestion was approved by hand raising of the members. However, each member has to approve that his/her data will be available in the website. For this reason, the record can be established only after the next round of payments of membership fees as the approval will be asked in the form for membership fees.

## 9. Major policy questions proposed by Board

## a) Patenting

The Board decided that ESHG will have a new Patening and Licencing Committee (PLC). It will consist 5-7 members of ESHG with Gert Matthijs as the Chair. The Committee will also have external experts from different disciplines. The Committee will work for 2 years.

#### b) Statutes

The Board has made a suggestion to modify the Statutes mainly to update and/or clarify some issues. The plan was that the modified version would be sent to the membership for voting and then brought to Membership meeting 2005 for final acceptance.

#### c) History of ESHG/human genetics

The Board decided to set up a "historical interest group". The Board invited Peter Harper to chair this group and Milan Macek and Christos Yapijakis to be members of the founding committee.

d) Award for Genetic Education

The Board decided to have Award for Genetic education every 2-3 years.

c) Topics for PPPC workshops

PPPC's recent topic was Pharmacogenetics and the coming topic is The interface between medically assisted reproduction and genetics.

#### 10. Close of meeting

The meeting was closed by Veronica van Heyningen at 19.30 hours. Minutes were taken by Secretary General Helena Kääriäinen, June 2004.

## **Report of the Publications Committee April 2005**



Prof. GertJan van Ommen

The EJHG is continuing to flourish. A major benefit of our liaison with Nature Publishing Group has been the highlighting of EJHG papers on various specific subpages of the Nature website – and incidentally even on the Nature home page. The authors in question are being duly informed of this. This not only meets with favourable reactions of authors who are pleased with the extra leg-up, but it also further increases the interest in submitting to the EJHG. We now receive typically 50 manuscripts per month. We have agreed with our publisher, Nature Publishing Group, to significantly expand the size of the journal from 1070 to 1270 pages. The first effect of this has already been the sheer size of the first issues this year, containing on average no less than 130 pages of copy.

Moreover, to eliminate the backlog caused by our increased submissions, the May issue has been made into a 'bumper', double spring issue of nearly 180 pages. While the Advance Online Publications system has in principle dealt with the backlog, from now on we aim to keep the delay between electronic and hard copy publication as low as possible, typically 2-3 months. To achieve (and maintain) this, we have become yet more demanding of the quality, general scope and potential impact of the manuscripts submitted. Even while this has unavoidably disappointed a number of our aspiring authors, this is part of the ongoing maturation of the EJHG and we are confident that this will result in a further increase in our Impact Factor

score. Other indications of the EJHG's rising impact are the about 35% increases of both Table-of-Contents registrations and page views of our website, as well as the significant increase of our subscriber basis in the US, all in the last year. Our publisher, NPG, also increased the feed back on the journal by organizing electronic consultations with the editorial board members and the readers. Content wise, a further significant improvement has been the introduction of a new EJHG copy category, "News and Commentary". This

section, in the front of the journal and well-discernible by its layout, covers items of relevance to the broad field of Human Genetics, presented in a format accessible to a broad readership, much like the "News and Views" found in Nature. These contributions, are being identified from the recent literature (or other newsworthy events), thus far mainly by the energetic activity of Nick Campbell, the Executive Editor Genetics of NPG but the readership is invited to contribute suggestions – of topics as well as authors - are welcomed at ejhg@lumc.nl. To deal with all this increased activity, we also have expanded our panel of Section Editors. We welcome four new Section Editors: Mark Daly (Boston, US) joined us in late 2004 as Section Editor for Statistical Genetics and Genetic Epidemiology. Markus Perola (Helsinki) has succeeded Leena Peltonen as Section Editor Genetic Epidemiology. Nicholas Katsanis (Baltimore, US) and Phil Beales (London, UK) will strengthen our review section as specific Reviews Editors. Of these, Phil Beales will take the Practical Genetics series under his wings. This series, started modestly last year, is now being set up more rigorously, involving a close collaboration with Orphanet, the brain child

of Ségolène Aymé, our section Editor Genetics Services and her team. It will be fired up in the second half of this year. Finally, like the previous years, the ESHG will honour at this years' Prague meeting the three EJHG citation top scorers of papers, published in 2003 and cited in 2004 (and the first two months of 2005). These awards are to stimulate the first authors in their further careers. The winners this year are: No. 1. Croucher, PJP et al. Haplotype structure and association to Crohn's disease of CARD15 mutations in two ethnically divergent populations (2003) EJHG 11, 6-16; No. 2. Bairead, E et al. Association of NOD2 with Crohn's disease in a homogenous Irish population (2003) EJHG 11, 237-244; No. 3. Musante, L et al. Spectrum of mutations in PTPN11 and genotypephenotype correlation in 96 patients with Noonan syndrome and five patients with cardio-facio-cutanesous syndrome (2003) EJHG 11, 201-206.

> Gertjan B van Ommen, Editor-in-Chief. Jean-Jacques Cassiman, Chair Publications Committee

## Activity Report of the PPPC

The PPPC is currently composed of Violetta Anastasiadou, Ségolène Aymé (chair), Suzanne Braga, Jean-Jacques Cassiman, Domenico Coviello, Gerry Evers-Kiebooms, Helena Kääriäinen (secretary), Gyorgy Kosztolanyi, Ulf Kristoffersson (Deputy-chair), Joerg Schmidtke, Jorge Sequeiros, Martina Cornel and Lisbeth Tranebjaerg.

During the past year, the PPPC dedicated its activities

- 1) to the finalisation of a document on pharmacogenetics
- 2) to the preparation of a document on "Reproduction and Genetics"

## The Pharmacogenetics report

A background document, summarising the professional and societal issues to be debated, was drafted under the supervision of Ségolène Aymé. It is based on the medical and scientific literature and on any other relevant document. More than 150 experts were asked to review it. A sub-committee was then invited to a two-day workshop of 50 participants (March 04) in Seville (Spain). This workshop was jointly organised with the Institute for Prospective Technological Studies, which is an EC joint research centre, and with EPPOSI the European Platform of Patients organisations, Science and Industry. Experts from all disciplines actively took part in the exercise and agreed on conclusions. The findings of this workshop

formed the basis of a report that will be published soon as a supplement of the European Journal of Human Genetics. The discussions during the workshop have been incorporated in the background document, which has been sent for re-review to the 150 experts in the field. The final document was put on the ESHG website for public consultation during summer 04.

The Assisted-Reproduction and Genetics report

The PPPC did the same exercise to explore the societal issues around the interface between assisted reproduction and genetics, in close collaboration with the European Society for Human Reproduction. The background document was prepared under the supervision of Helena Kääriäinen and sent for review to a large set of experts. Fifty of them were invited to a workshop which took place on 31 March-1 April 2005 in Seville, Spain. It was co-organised by ESHG, ESHRE and the Institute for Prospective Technological Studies, a joint research centre of the European Commission.

The workshop was extremely useful and productive. We all learned a lot, what really points to the utility of interdisciplinary meetings. Recommendations were drafted at the end of the workshop. They are currently under review before being submitted to the ESHG board in Prague. Both the background document and the proposed recommendations will be open for discussion on the website of the ESHG from June to August 05. It is expected that there will be a co-publication (ESHG and ESHRE) of the document later this year.

The next topics to be explored are still in discussion and will be presented at the membership meeting in Prague.

## **INTERNATIONAL FEDERATION OF HUMAN GENETICS SOCIETIES**

http://www.ifhgs.org

The Executive Committee of the IFHGS compiles representatives of the full member societies: European Society of Human Genetics (ESHG):Jean-Jacques Cassiman and Veronica van Heyningen; American Society of Human Genetics (ASHG): Robert L. Nussbaum, Judith Allanson and Elaine Strass; Human Genetics Society of Australasia (HGSAA): John MacMillan and Eric Haan; Latin American Network of Human Genetics Societies (RELAGH): Jose Maria Cantu and Roberto Giugliani; East Asian Union of Human Genetics Societies (EAUHGS): Takehiko Sasazuki

The IFHGS grows continuously and is well on its way to be represented on all continents. New corresponding and affiliate members have joined in the past year; please visit: http://www.ifhgs.org Of course, an important activity will be the next International Congress in 2006.

International Congress of Human Genetics, Brisbane, August 6 - 10, 2006



Ségolène Aymé

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Preparations are in full swing and the scientific program is close to being finalized. Support for student fellowships is being sought by the different member societies. http://www.ichg2006.com/

## **Future Meetings**

The meeting 2011 will be hosted by the ASHG and held in Montreal. The EAUHGS has offered to host the meeting 2016 in Kyoto. ReLAGH has also expressed interest. Proposals will be accepted through the end of 2005.

## **Future Members and Associate Members**

The International Genetic Alliance (IGA) would like to have a one-day meeting in Brisbane to be held at the same time as the scheduled scientific sessions.

The Asia Pacific Human Genetics Society has not quite completed its creation. The plan is to present an application in 2005.

The African Society of Human Genetics (AfSHG) asked for consideration to become a full member society. India and Pakistan: a regional group is being created. The group would include Sri Lanka and Iran. More is planned for 2005.

Egypt will be contacted and asked to join.

### **Educational Initiatives**

The idea of developing an itinerant medical course in human genetics is being considered. It would be held in a different location each year. Funds would be sought from governments to be used for faculty support and student scholarships. Brazil has asked for support to pay ten professors for teaching human genetics in poorer countries.

Teaching bioethics is another possibility. One way to start this initiative would be to design a pilot program in one region and then use it as a model.



Prof. Jean-Jacques Cassiman

Liaison officer for the ESHG, Jean-Jacques Cassiman

## SPC Report for 2005

Following the successful Munich 2004 meeting, the SPC met one time in July 2004 to agree on invited speakers and plenary sessions for the Prague meeting. It was decided to have 13 concurrent sessions rather than the usual 9, because the conference is growing steadily in number of attendees. The SPC met again in February 2005 to review 1500 abstracts and to select the 78 most suitable for oral presentation It was decided to present the first ESHG teaching award to Professor Giovanni Romeo in recognition of his creation of the European School of Medical Genetics, which has organized the Sestri Levante and Bertinoro meetings for many years with continuing success in teaching students from all over Europe at the highest level.

Furthermore, it was decided that Professor Stylianos Antonarakis will receive the ESHG award for his ground-breaking work in many fields of human genetics, notably the functional effects of aneuploidy and the unraveling of the complex genetic basis of psychiatric diseases.



Prof.Han Brunner

For the meeting in Prague 2005, members of the SPC included Han Brunner (Chair), Milan Macek Jr (local host), Cornelia van Duijn, Karl-Heinz Grzeschik, Stanislas Lyonnet, Jean-Louis Mandel, Andres Metspalu, Andre Reis, Gudrun A. Rappold, Andrew P Read, Niels Tommerup, Gert Jan van Ommen, Peter Lichter, Juha Kere, and Paulo Gasparini.

Helena Kääriäinen joined us as Secretary-General of the ESHG.

After the Prague meeting, Niels, Jean-Louis, Karl-Heinz, Gudrun, and Andrew will leave the SPC. We thank them for always being here and bringing their many ideas and insights to the committee. Andrew Read's contribution was especially great in creating the best possible programme in Human Genetics in Europe. We are very happy that he will continue to be involved as President of the Annual Meetings Committee and as Treasurer of the Society.

We welcome new SPC members for the Amsterdam meeting 2006: Raquel Seruca, Mariano Rocchi, Andrew Wilkie, Brunhilde Wirth and local host Peter Heutink.

Han G. Brunner, chair of the SPC

## **ESHG-EDUCATION COMMITTEE**

This is the newly appointed Education Commission (November 2004)

Domenico Coviello (Chairman, Milan, Italy), coviello@unige.it Celia DeLozier (USA/Switzerland), cddelozier@comcast.net Peter Farndon (Birmingham, UK), p.a.farndon@bham.ac.uk Tiemo Grimm, (Wurzburg, Germany), tgrimm@biozentrum.uni-wuerzburg.de Rodney Harris (Manchester, U.K.), rodney.harris@man.ac.uk Shirley Hogdson (London, U.K.), s.hodgson@sghms.ac.uk Alastair Kent, (Patients Organizations, GIG and EAGS), alastair@gig.org.uk Gyorgy Kosztolanyi (Pécs, Hungary), Gyorgy.Kosztolanyi@aok.pte.hu Jorge Sequeiros (Porto, Portugal), jsequeir@ibmc.up.pt Heather Skirton (Plymouth, UK), heather.skirton@plymouth.ac.uk



Domenico Coviello, MD, Ph.D.

The first committee meeting was in Strasbourg (2002) with the aim to foster the formation of networks interested in genetics education, counselling and testing issues. Celia DeLozier chaired the committee the first two years.

In the first year the committee set up interaction with the already established initiatives: a) Educational courses of EGF (European Genetic Foundation); b) Liaisons with the study on education practice and policies of general practitioners or of non-geneticists in Europe by GenEd.

In the second year members of the committee were active in two initiatives: a) Participation in the EC Network of Excellence EUROGENTEST (Integrated Network for test development and harmonization of quality of genetic testing services in Europe); b) Set up a questionnaire for heads of departments to assess programs for post-graduate education already in place. We have info on 45 programs from 13 countries, but we expect answers from several other University/Centres. A web page with a list of the relevant programs is on the ESHG page.

In the third year the work planned includes: a) Coordination of/with ongoing EU projects involving education; b) Establishment of a network of resource individuals in Europe, both for professional and for patients organizations, that will help the committee to collect information on genetic programs in each of the 25 EC countries; c) Convene a meeting by the end of the 2005 of national coordinators to identify the relevant professional groups, to analyze materials and define the baseline competences. The meeting will be supported by the EUROGENTEST project (www.eurogentest.org).

## Of interest:

European Symposium of Genetic Education for Non-genetic Health Professionals, Friday, 6th May '05; Satellite at European Society of Human Genetics Meeting, Prague. (http://www.medicine.manchester.ac.uk/gened/healthcaregeneticseducationpraguesymposium/)

May 8th, 13.15-14.45 hrs, a Genetic Education workshop will take place at the ESHG meeting.

Domenico Coviello, MD, PhD.

## Report from the Patenting and Licensing Committee (PLC)

The Patenting and Licensing Committee (PLC) was installed last year in June, because the ESHG wants to play an active role in the current discussions on patenting and licensing of genes, sequences and genetic tests. The PLC has to become a forum where the specific issues and problems can be discussed, and experts can be invited. In a proactive way, via the work of the PLC, the ESHG wishes to prepare and propose solutions to disputed matters and be available for advice to lawmakers and courts. It is also a matter of involving the genetics community in the analysis and the discussions on the practical, political, societal, ethical and economical aspects of patenting and licensing. The PLC has taken a slow start. As a chairman of the PLC, I admit that I have been rather late in getting it rolling. In the aftermath of the BRCA case, several urgent matters have popped up, which have required a quick (and often late) reply, not allowing us to fully inform all colleagues or to gather a response from all interested in the field. The main

issues are summarized below. Also, right from the start, I promised the Board that I would not mingle my appointment to the PLC with my activities in the BRCA patents opposition. As you will read in a separate section in this Newsletter, a lot has happened in the past year with the BRCA patents – and there are still only 24 hours in a day.

Thus far a few ESHG members have volunteered for the PLC: Prof. Gert-Jan van Ommen (who agreed on the very first day), Dr. Ugur Ozbek, a young geneticist from Istanbul University and Dr. Milan Macek Jr. from Prague. In addition, Dr. Ségolène Aymé will warrant the liaison with the Professional and Public Policy Committee (PPPC). But there is room for additional 2 to 3 members. Thus far, the discussions have taken place via email. In due course, the team will identify a comparable number of external experts from different disciplines and representing interested stakeholders, to also take part in the discussions. It is our aim to meet once or twice a year.

Nevertheless, several things have happened in the field of patenting and licensing of genes.

1. Art 52(4) EPC – towards an exemption on genetic diagnostic testing? The ESHG has responded to a 'call for comments 'from the European Patent Office (EPO) to the interpretation of the term "diagnostic

methods practised on the human or animal body" within the meaning of Article 52(4) of the European Patent Convention (EPC). (See: <a href="http://www.european-patent-office.org/news/info/2004\_04\_08\_e.htm">http://www.european-patent-office.org/news/info/2004\_04\_08\_e.htm</a>). This article from 1973 excludes "diagnostic methods, practiced on the human or animal body" from patenting. Interestingly, the EPO came to the conclusion that different Boards of Appeal (the instances within EPO that decide on appeal procedures) have interpreted this legal article in different ways, whereby patents on diagnostic methods that have been accepted in some cases, could have been revoked if judged by a different. This of course leads to legal uncertainty. It is in this context that the President of EPO has asked the highest instance of the organization, the Enlarged Board of Appeal, to clarify this matter. The Enlarged Board of Appeal has called for comments until August 2004.

This was all short notice and it came even before the PLC could be reasonably established, but nevertheless, I felt that we as geneticists – and preferably the ESHG as our professional society – should try and take part in the discussion.

I personally believe that a call to exclude gene-based diagnostics from patenting is legitimate from the standpoint that the patenting system should not interfere with the availability of a genetic test for the patient, a measure that could logically be extended to other diagnostic methods characterized by the absence of "invent around" options. The definition in Art. 52(4) EPC dates back to the days when people did not want surgical methods and other medical practices to be patented in order not to block a medical professional to help people in need.

This could be updated to include genetic testing. Even if Art. 52(4), as it stands now, does of course not deal with genetic testing per se, it was felt that, if the EPC has decided years ago that those who carry out surgical, therapeutic or diagnostic methods as part of the medical treatment of humans should not be inhibited by patents, it may well consider or install an analogous exemption on (germ line) genetic testing.

This broader interpretation of Art. 52(4) is a way to avoid monopolies on the use of a genetic sequence for diagnostic purposes in humans, without interfering with patent protection of other genetic applications, including the development of therapeutics. It would only apply to those patents in which a link between a (set of) mutation(s) in one (or more) gene(s) is claimed in relation to a disease, whereby commonly known technologies are proposed for its detection. It should of course not apply to inventions that improve the technical aspects of molecular diagnosis. Similarly, the technical improvements that have allowed the manufacturing of chips and many other new methods for mutation detection should remain patentable.

I have done most of the practical work, together with a legal advisor, with limited opportunities to consult my colleagues during these last days of summer. The result is a very technical piece of work, in which we proposed a novel interpretation of Art. 54(2) that could contribute positively to the ongoing discussion on patenting of diagnostic. The work has incurred no costs for ESHG and was of course also not presented as a statement from ESHG, because we had not been able to consult the membership. Nevertheless, I hope that it will have an impact on the EPO's evaluation of the problem. The outcome of the discussion at EPO has not been released yet.

## 2. Trilateral Workshop on Intellectual Property Rights in Genomic and Protein-Related Inventions

This workshop was organized by the Committee on Intellectual Property in Genomic and Protein Research and Innovation, and a joint activity of the Science, Technology, and Economic Policy (STEP) Board and Science, Technology and Law Program of the National Academies of the United States (NAS), at the Rockefeller Foundation Center in Bellagio, Italy, December 13-17, 2004. (see: <u>http://www7.nationalacademies.org/STEP/</u> and <u>http://www7.nationalacademies.org/step/proteomics\_agenda\_12\_2004.pdf</u>)

The meeting is actually part of a series of consultations by the NAS on this matter. At this meeting, the organisers brought together a selection of experts in the different fields from the U.S., Europe and Japan (hence 'trilateral'). The genetics research community was represented by Dr. Bob Waterston and Sir John Sulston. I was invited to assist to the meeting and to give provide insight in the field of genetic testing in Europe and some background to the BRCA gene patents oppositions in the session devoted to 'The Impact of Patenting and Licensing on Genetic Testing Services and Recommended Changes in Policy'. The NAS is considered the most important and objective voice for science policy in the U.S. They will develop an important report for the U.S. Government in the course of 2005. I am glad that I was able to present a 'European genetic-diagnostic' view at this meeting and I have of course mentioned that the ESHG has an interest in these matters as well.

## 3 Compulsory licenses

An alternative to filing oppositions is to find and use safeguard measures for the exploitation of patents. Indeed, Europe lacks a system that ensures guidance and surveillance of licensing of genetic inventions. The 'compulsory licensing' system is the traditional safeguard against excesses in licensing and most countries have regulations for granting such licenses. It is a system whereby a (national) committee or court obliges a patentee to grant a license to a user, at a fair expense. However, the existing legislation is not well equipped to protect the patients and the public health care system from the potentially negative effects of a monopoly. For instance, one can only obtain a compulsory license in Belgium when is has been shown that the patent owner has not been exploiting his monopoly rights for 4 years, and on the condition that one is not infringing the patent. Patients cannot wait for 4 years to get a test.

The French government has included in its 'Loi relative à la bioéthique' a 'licence d'office' which would be decided upon by the Minister of Health in cases where the use of the patent invention would be important for the provision of public health services and where the patent owner and the user have not been able to establish a licensing agreement. This 'ex officio' license would be applicable to diagnostic methods. The Lower House of the Belgian Parliament has recently (10 March 2005) passed a bill transposing the Directive 98/44/EC into the Belgian law, in which a similar licensing system has been included. It would be interesting for the other countries to consider this simplified system for compulsory licensing, or to at least compare it to the existing system.

## 4 'Guidelines for the Licensing of Genetic Inventions' from the OECD

The Organisation for Economic Cooperation and Development (OECD) has undertaken work in the field of licensing and biotechnological inventions. Specifically, the OECD has been developing draft 'Guidelines for the Licensing of Genetic Inventions'. The OECD has undertaken consultations with respect to these draft guidelines and was interested in the input of a wide spectrum of stakeholders. The OECD was accepting comments from February 1st to March 11. The information is available on the OECD website at www.oecd.org/sti/ biotechnology/licensing.

The draft guidelines have been circulated to the members of the PLC early in March, and they have returned their comments, but of course, it has not been possible to submit comments on behalf of the ESHG, due to the time constraints. However, the PLC will organise some more discussions about these guidelines. As there are good contacts between several members of the PLC and the people at OECD, we will have the opportunity to raise additional comments in the later phase of the preparations.

In brief: these guidelines are already the result of lengthy discussions at the OECD, and they were found to be fairly well balanced. We support the guideline that license agreements should not lead to exclusive control over individual genetic information. We were happy to see that – even if exclusive licensing is legally acceptable in the field of patenting and licensing – the guidelines put a strong emphasis on this aspect. Other issues in these guidelines concerned for instance a call to exclude excessive up-front payments for licensing.

## 4. Further reading...

Finally, I want to draw your attention to a recent article in Science, in which 74 US patents on genes have been analysed in detail. It was shown that 38% of the claims in these patents were problematic, in terms of

description, enablement or utility, novelty and definiteness. The conclusions are not very flattering for the US Patent and Trademark Office (USPTO). (See: Paradise et al. Patents on Human Genes: an analysis of scope and claims. Science, 307: 1566-1597, 2005). The situation is probably better in Europe because the EPO has the reputation to be more stringent in the examination of patent applications.

Gert Matthijs, April 15, 2005

## The BRCA1 and BRCA2 gene patent oppositions

The oppositions against the patents on the first breast cancer gene, BRCA1, have recently been concluded. These oppositions, which had jointly been filed by different national genetic societies and research institutes, and other parties including the Dutch and Belgian governments, were directed against the 3 patents on the BRCA1 gene, which had been granted in 2001.

Patents can be opposed on the basis of non-conformity with the basic patentability requirements. Most commonly the reason for opposition is 'lack of inventive step', 'lack of novelty' and 'lack of disclosure'. Additionally, opposition may be based on the disclosure not being sufficiently clear and complete, or on extension of the subject-matter covered by the granted claims beyond the content of the application as originally filed.

The oppositions were mainly fuelled by the geneticists and institutes who wish to be able to offer breast cancer testing within the framework of the public health care system. To stop testing was an alternative, which was quickly dismissed by most laboratories. The cost of the commercial test – not reimbursable in most countries – would exclude a large group of women from testing.

The first BRCA1 patent EP 699754 is a use patent: it asserts rights over the diagnostic use of the BRCA1 gene, whatever the technique chosen at the laboratory. The main claim read as follows: "A method for diagnosing a predisposition for breast and ovarian cancer in human subject which comprises determining in a tissue sample of said subject whether there is a germline alteration in the sequence of the BRCA1 gene coding for a BRCA1 polypeptide having the amino acid sequence set forth in SEQ. ID. NO: 2 or a sequence with at least 95% identity to that sequence, said alteration being indicative of a predisposition to said cancer."

Admittedly, it has to be said that the full BRCA1 sequence was not available prior to late 1994. But there were 9 'errors' in the BRCA1 sequence initially submitted by the inventors in November 1994. There is substantial jurisprudence at the European Patent Office (EPO) that reference sequences have to be correct. The patentee has argued that the errors in the early priority filings were polymorphisms. However, the opponents could convincingly show that they were not, and that they were correct in the filing of March 24, 1995. Hence, this became the new priority date. By this date, a 'method for diagnosing a predisposition for breast and ovarian cancer based on the BRCA1 gene' was no longer an invention: it had been published in literature in October 1994 and practiced in different laboratories. Consequently, the Opposition Division of the EPO revoked the patent in its entirety, on May 19, 2004.

This was good news. Nature headlined: 'Clinicians win fight to overturn patent for breast-cancer gene' (Abbott A., Nature 429:329, 2004).

The second BRCA1 patent EP 705903 is a product patent that asserts the rights over the isolated BRCA1 gene and a handful of mutations found to be causative for familial breast and ovarian cancer. The first claim reeds as follows: "An isolated nucleic acid which comprises a coding sequence for the BRCA1 polypeptide defined by the amino acid sequence set forth in SEQ. ID. NO: 2, or an amino acid sequence with at least 95% identity to the amino acid sequence of SEQ. ID. NO: 2."



The third BRCA1 patent EP 705902 is a product patent covering an additional set of mutations related to familial breast and ovarian cancer and their use in a method for diagnosing a predisposition for breast and ovarian cancer.

In January 2005, these 2 patents were maintained after the final hearings, but in amended - say slimmed - form: they no longer include a method for diagnosis, but only relate to a probe for the BRCA1 gene and a probe for the common Ashkenazi 185delAG mutation, respectively.

This time, Nature concluded: 'Europe pares down double patents on breast-cancer gene' in 'battles worthy of a TV court drama' (Abbott A., Nature 433:344, 2005). Indeed, these were exciting times in Munich, but the decisions of the EPO were overall very favourable for breast cancer diagnostics. The amended patents do no longer constitute a threat to BRCA1 testing in Europe.

But the patent owners have filed an appeal against these decisions, so the threat is not fully over yet.

The patent on the second familial breast and ovarium cancer gene, BRCA2, was granted to Myriad in 2003. This patent EP 785216 is a product patent on the most frequent allelic variant of the BRCA2 gene, several identified disease mutations in the BRCA2 gene and the method for determining variation of the nucleotide sequence of a suspected mutant BRCA2 allele associated with predisposition to breast cancer in reference to this most frequent allelic variant of the BRCA2 gene. The oral hearing before the Opposition Division will take place in Munich on June 29, 2005.

More details on the outcome of the recent BRCA1 patent oppositions will be given in the special session on "The success of the oppositions against the BRCA1 patents: how did it occur and what will be the impact on genetic testing?" on Sunday, May 8, 2005 at 10.45. At the session, the authors will also try to look beyond the 'Myriad case'.

The detailed information on the patents and the minutes of the opposition proceedings are available for consultation in the Online Public File Inspection at http://ofi.epoline.org/view/GetDossier

The European Patent Office has issued several press releases: "Myriad/breast cancer" patent revoked after public hearing' (http://www. european-patent-office.org/news/pressrel/2004 05 18 e.htm May 18, 2004), 'Patent on breast and ovarian cancer susceptibility gene amended after public hearing' (http://www.european-patent-office.org/news/pressrel/2005 01 21 e.htm, January 21, 2005) and 'European patent on mutations in breast and ovarian cancer susceptibility gene amended after public hearing' (http://www.european-patent-office. org/news/pressrel/2005 01 25 e.htm, January 25, 2005).

Gert Matthijs

# **ORPHANET** the European information resource on rare diseases and related activities

www.orpha.net

Orphanet is a database of 3,760 rare diseases (which includes all genetic diseases) and orphan drugs for all publics. Its aim is to contribute to the improvement of the diagnosis, care and treatment of patients.

## The Orphanet Encyclopaedia

Orphanet provides access to an encyclopaedia which is a comprehensive collection of more than 400 review articles on rare diseases and of 1308 short texts. It is an author-based, peer-reviewed online publication written in English. The abstracts are progressively translated to be available in 5 other languages: French, Italian, Spanish, German and Portuguese. This encyclopaedia will become soon an open-access journal with BioMedCentral.

### The Orphanet directory of services

Orphanet also provides information on specialised outpatient clinics, clinical laboratories, research activities, clinical trials, registries, networks and support groups in Europe. Orphanet is the most comprehensive database of genetic

testing laboratories available to date. The information is going to be expended as to meet the requirements of the EuroGenTest project.

### The Orphanet consortium

Orphanet is run by a consortium of European partners, the French one being the project manager. Currently the following national teams are actively participating:

Austria: Dr Till Voigtländer - Belgium: Pr Jean-Pierre Fryns – Bulgaria: Pr Emil Simeonov - Cyprus: Dr Violetta Anastasiadou – Denmark: Pr Karen Brondum-Nielsen - Estonia: Pr Andres Metspalu - Finland: Pr Helena Kääriäinen - France Dr Ségolène Aymé (project manager) - Germany: Pr Joerg Schmidtke - Greece: Dr Lina Florentin-Arar - Hungary: Pr Gyorgyi Kosztolanyi - Hungary: Pr Andrew Green -Italy: Pr Bruno Dallapiccola – Lithuania: Pr Vaidutis Kucinskas – Netherlands: Pr Martina Cornel – Portugal: Dr Margarida Reis-Lima – Romania: Pr Mircea Covic – Spain: Dr Miguel Del Campo – Switzerland: Dr Loredana d'Amato Sizonenko -United-Kingdom: Pr Dian Donnai.

### **Orphanet** services

Orphanet is also providing several additional services:

A **search by clinical sign** facility has been designed to facilitate diagnosis. This service is available exclusively for dysmorphic syndromes (about 2300 syndromes) and not for the entire set of rare diseases.

A facility allowing patients to **register as a volunteer** to participate in research projects, including clinical trials has been designed. This service aims at speeding up the enrolment of patients in clinical research.

OrphaNews-Europe is a **monthly newsletter**, which provides scientific and political information about rare diseases and orphan drugs. Registration is free of charge and available on the home page website.

**OrphanXchange** (www.orphanxchange.org) is a database of molecules with a potential orphan indication, and of research projects with an identified potential for being developed for the diagnosis or the treatment of rare diseases. It is intended to speed up the development of diagnostic and therapeutic solutions for rare diseases.

## **Orphanet** funding

Orphanet was established in 1997 by the French Ministry of Health and the **INSERM** (<u>www.inserm.fr</u>). Both agencies are still funding the core project.

The European Commission is funding the encyclopaedia and the collection of data in European countries (since 2000 **DG Public Health and Consumers Protection** (<u>http://europa.eu.int/comm/health/index\_en.htm</u>) grants No S12.305098; S12.324970; SPC.2002269-2003220 and since 2004 **DG Research** (<u>www.cordis.lu</u>) grant No LSSM-CT-2004-503246). Several other sponsors are also funding Orphanet services:

## **Orphanet users**

Orphanet is visited daily by more than 10,000 users from 130 countries. The patients and their family represent one third of the visitors and the health care providers half of them. The others are scientists, teachers, students, journalists or Industry people. Half of the visitors come for the first time and have discovered the site through a web search engine. The others come regularly (13% more than twice a week). Among the users, 7.4% use also GeneClinics, 21.5% use OMIM and 36.2% PubMed.

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Segolène Aymé, Director of The ORPHANET Consortium

## Medical Genetics in Russia

The earliest research and public activities in human and medical genetics in Russia may be traced back to early 1920s, when N.K. Koltzoff in Moscow and Yu.A. Philipchenko in Petrograd (now St.-Petersbourgh) published their first papers on the inheritance of some traits in human families. In 1929, Russian neurologist and geneticist S.N. Davidenkov has founded the first genetic counselling unit in the World in Moscow and then formulated the principles of organization of genetic aid in hereditary neural diseases. Since mid-1930s, and through the following two decades, Russian geneticists suffered the dark period of Lysenkoism during which any sign of activity in genetics was not allowed in the Soviet Union. The "first swallow", as we say in Russia, of the coming summer in Russian medical

genetics was the publication of V.P. Efroimsson's book "The Introduction to Medical Genetics" (1964). Also in the 1960s and the 1970s a number of survivors of Lysenkoism (A.A. Prokofieva-Belgovskaya, A.A. Malinovsky, E.E. Pogosyanz, E.F. Davidenkova) together with then young scientists and physicians (N.P. Bochkov, A.F. Zakharov, L.O. Badalyan, M.E. Vartanyan, Yu.E. Veltischev and some others) tried hard to renew medical genetic research and practice in the USSR. Especially relevant was the organization of the Institute of Medical Genetics in 1969 (first director –Prof. N.P. Bochkov) by the USSR Academy of Medical Sciences in Moscow, later (1989) transformed into The Research Centre for Medical Genetics (first director – Prof. (now Professor emeritus) V.I. Ivanov); since 2004 the director of the Centre is Prof E.K. Ginter.

An important input to the creation of a genetic aid system in the USSR was made by the Department of Genetic Counseling of the former Institute of Medical Genetics (especially under leadership of Dr. S.I. Kozlova). In the 1970s and 1980s research staff of the department

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elaborated the scientific principles of general and specialized genetic counseling, the methods of computing the genetic risk and estimating the effectiveness of medical genetic aid. This and other departments of the institute/centre took active part in elaboration for the Ministry of Health of the Soviet Union (later – Russian Federation) of the Genetic Service in this country and the main documents regulating its due operation.

Of distinct value are the methods of biochemical screening for amino- and organic acids and computerized search and diagnostic systems for genetic and chromosomal diseases, both elaborated in the center, as well as the protocols of DNA-diagnostics and their actual performance for several dozens of genetic diseases.

At the beginning of the 21st century, Russian Federation had 84 regional, 10 inter-regional genetic counseling units and 7 federal centers for medical genetics, the latter mostly functioning within the leading research and educational centers subordinated to either the Russian Federal Ministry of Health or the Russian Academy of Medical Sciences. Total staff of the medical genetic units includes about 200 physicians-geneticists, 160 physicians-cytogeneticists and 130 physicians-biochemists.

Genetic service in Russia is aimed mainly at the prevention of most common and important forms of hereditary diseases, especially the programs of newborns screening for PKU and inborn hypothyreosis, as well as family counseling and staff education. 240 to 300 thousands of outpatients and families visit genetic counselors every year. Special attention is given to prenatal diagnosis of genetic and inborn diseases: more than 370 thousands of pregnant women are yearly subjected to US-observation and a fraction of those with genetic indications progressively increasing. Serum marker analyses are yearly made to more than 300 thousands of pregnant women. About 4500 to 5000 invasive prenatal diagnosis are carried out in Russia every year. Application of the above methods allows the revelation of up to 3500 - 4000 various developmental defects yearly, including 3000 to 3500 cases of congenital malformations and 150 to 240 cases of chromosomal anomalies. Following medical genetic findings, up to 3500 pregnancies are terminated every year. Further progress in practical applications of medical genetics is rather slow due to limited funding and, thus, too moderate development of genetic aid system in Russia. Only a few universities organized medical genetics departments or teach special courses in genetics at some other departments. Resources of research centers are also to be exploited to a larger extent in staff training and certification, especially of such major centers as the National Research Centre for Medical Genetics of the Russian Academy of Medical Sciences in Moscow (Director - Prof. E.K. Ginter), Institute of Medical Genetics of the Siberian Branch of the Academy in Tomsk (Director - Prof. V.P. Pouzyrev) and the genetic and paragenetic units of the Research Institute of Obstetrics and Gynecology of the North-West Division of the Academy (Director - Prof. E.K. Aylamazyan, principal geneticist - Prof. V.S. Baranov). Physician's training in medical genetics is carried out by the Academy of Postgraduate Physicians' Education in Moscow (Chair of Medical Genetics is headed by Prof. S.I. Kozlova).

Of great help to a smooth running of medical genetic research and practice is the Russian (former USSR) Society of Medical Geneticists, uniting about 500 members and holding its meetings every five years (the next, 5th, meeting is to be carried out this May in Ufa). Recently, research projects in medical genetics and genetic counseling in Russia are focused mainly at the elaboration of diagnostic protocols, risk estimation on the basis of molecular genetic evidence, interrelations of genetic units with other health services and the monitoring and prevention of inborn birth defects. Unlike most developed countries, only a few studies were carried out in Russia on the ethical, psychological and legal aspects of medical genetics (e.g. V.I. Ivanov, V.L. Izhevskaya, L.F. Kurilo and some others). Photos Russia 1-3



Three successive directors of the Institute/ Centre for Medical Genetics in Moscow: Prof. N.P. Bochkov (left), Prof V.I. Ivanov (right), Prof E.K. Ginter (middle).



Prof. N.P. Bochkov's (lower row, left) team of medical geneticists: Prof. N.P. Kuleshov (lower row, right), Prof A.N. Chebotarev (upper row, left) and Prof. V.S. Zhurkov (upper row, right).



A group of Russian medical geneticists at a meeting.

# European Society of Human Genetics

# April 2005 / Newsletter No. 12

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## Editor's Message



Lina Florentin-Arar, B.Sc., Ph.D.

It has been two years since I got involved as the co-editor and later as the editor of the ESHG Newsletter. It is only this year, however, that I have been without the valuable help of Patricia who knew all the details and directed me. I am therefore especially thankful to both our Secretary General Helena Kääriäinen and Jerome del Picchia from Vienna Medical Academy for their help.

I think that I now have earned enough experience so that I can pursue a new vision for the ESHG Newsletter. For this I need your contributions as members of our Society. I was looking at all the reports of the activities of the committees and I felt that we are a very active Society. Education, education to non-geneticists, quality control issues, patenting, public and professional policy issues, efforts to have our specialty recognized on a European level for both clinical and laboratory geneticists, an exciting Scientific Journal, links with the International Genetics Community etc. An invaluable legacy and an amazing effort to teach, to inform and harmonize all issues related to medical genetics across Europe and promote science and ESHG.

And yet there are so many issues that are still to be explored in a continent where history, financial and educational status, mentality, laws and country policies vary so much as can very clearly be seen in our series on Medical genetics in different European countries. There is a lot we all could learn from other countries, and a lot that we still do not know.

Genetics is a new and evolving field, constantly changing, controversial at times and exciting. It is not only the science but also the application and integration of every discovery into our health systems and our societies that has brought sometimes also mistrust on the part of other professionals who feel threatened, the media, the public, the state. When, however we exchange information and opinions amongst the different countries we can learn from each other and help each other.

I therefore decided to send an invitation letter to all the Human Genetics Societies not only in Europe but across the world welcoming them to contribute to our Newsletter.

The Newsletter would be very interested to have information on events that take place in the field of Medical Genetics in your country, local meetings of special interest to all the European and international genetic community, local discussions and public debate, new laws, committees and actions around the bioethics of Medical genetics, interesting sites related to genetics and a lot of other things near to our field.

Please help me to make the Newsletter a floor of discussion on all the burning issues related to our Science. Exchanging information amongst the different countries will help to promote Medical Genetics in Europe and everywhere.

Articles are welcome at the Editor's e-mail lflorentin@leto.gr

Lina Florentin-Arar, B.Sc., Ph.D.