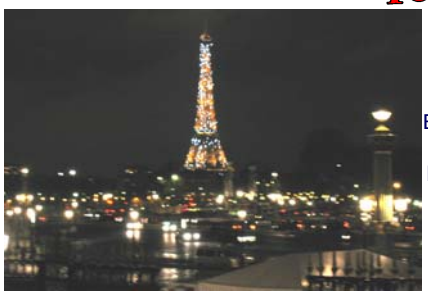
European Skeletal Dysplasia Network
www.esdn.org
EC contract #QLG1-CT-2001-02188

Issue 4
January 2004

A Happy New Year!

ESDN Newsletter



Beautiful Paris, by night

Editorial

The main focus of this fourth issue of the ESDN Newsletter will be to update you on ESDN activities, including:

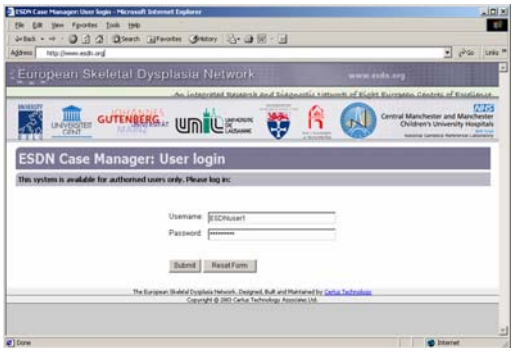
The development of the Web-portal system - if you would like to become a user please let us know, email: info@esdn.org stating your full mailing address with telephone and fax numbers.

Mike Briggs (ESDN Manchester-Research) will give a summary of the ESDN MTR meeting.

Rob Elles (ESDN Manchester-Diagnostics) will tell us about the ESDN EQA scheme which was introduced last year.

Also this issue's "ESDN in focus" comes from the Newcastle Research group, the focus of their work is on the chondrodysplasia, Ellis-van Creveld syndrome (EvC).

Update on ESDN activities



Website The ESDN electronic Communication, Management and Web-portal system (ESDN-CMW) is a secure interactive website which allows us to manage ESDN diagnostics to a high level of efficiency whilst at all times protecting the confidentiality of all patient referrals and ensuring that adequate consent procedures are in place.

- Registered users can submit case histories and radiographs directly to ESDN using this system.
- Relevant information for each case will automatically be referred to a panel of skeletal dysplasia experts who will discuss the case and either confirm the diagnosis or provide a differential diagnosis.
- Once a diagnosis has been agreed, DNA will be requested from the referring clinician and sent to the appropriate laboratory for genetic analysis.
- The referring clinician will be kept aware of the referral process at all stages and receive by e-mail any requests for further information or appropriate samples.
- Results of the molecular testing will be issued directly to the referring clinician through the ESDN-CMW.

Full official use of this system, to registered users, will begin in February. For further information please contact Jacky Taylor, email: info@esdn.org

MTR Members of ESDN gathered in Paris on December 1st 2003 for a mid-term review of the project. This meeting was also attended by Dr Elmar Nimmesgern, our project officer from the European Commission, and Dr Christian Kasperk, who had kindly agreed to act as an external expert. Thanks to much hard work by all members of ESDN the review went very well and in the New Year we were happy to receive a recommendation to continue the project unchanged.

Participants of the MTR Meeting, December 2003 Paris, France

ESDN EQA

External Quality Assessment (EQA) is an important part of ensuring the accuracy and quality of genetic tests. The ESDN EQA scheme is being developed by ESDN in conjunction with the European Molecular Genetics Quality Network (EMQN) & the United Kingdom National External Quality Assessment Service (UKNEQAS), to bring ESDN labs into line with many genetic centres in Europe that are participating in EQA schemes.

To date we have collected and successfully validated around 50 samples for ESDN EQA and the first batch of cases have been sent out to ESDN labs to check their performance.

To learn more about EQA systems see www.emqn.org

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ESDN in Focus

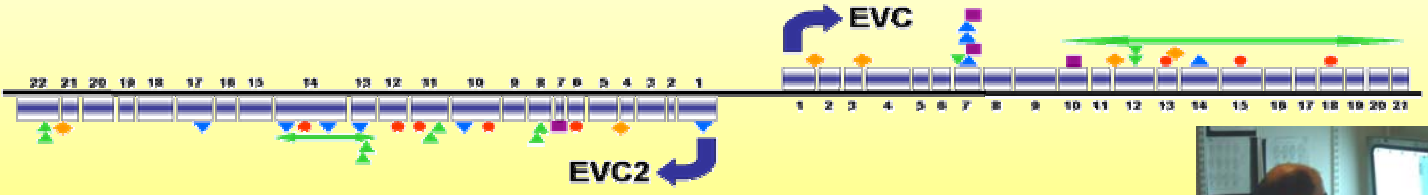
Part IV: "Details on the Newcastle Research group"

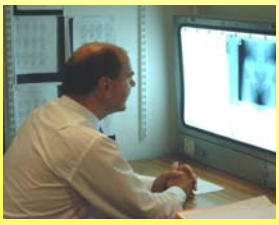
The Newcastle ESDN-Research component is based in the Institute of Human Genetics (http://www.ncl.ac.uk/ihg/) at the International Centre for Life (http://www.centreforlife.co.uk/). The research, headed by **Judith Goodship**, focuses on the chondrodysplasia, Ellis-van Creveld syndrome (EvC).

EvC is an autosomal recessive chondrodysplasia with a wide spectrum of developmental defects. Patients display distalward shortening of the limbs, short ribs, postaxial polydactyly, multiple frenulae between the lip and gum, dysplastic teeth and nails, and 60% have a cardiovascular malformation, usually an atrial septal or atrioventricular septal defect.

We have identified 2 novel genes that lead to EvC when mutated, *EVC* and *EVC2*. These genes are organised in a head-to-head configuration, with potentially shared regulatory elements, a formation that has been evolutionarily conserved between man and fugu.

Current research is aimed at elucidating the functions of these two genes during development.





- **Dr Michael Wright** has diagnosed a major proportion of our EvC patient collection. He is currently re-assessing the clinical phenotype of EvC with an interest in any differences caused by mutations in either EVC or EVC2.
- **Dr Victor Ruiz-Perez** is producing a mouse model for EvC by gene knockout. He is also studying the tissue distribution of EVC/EVC2 during mouse embryogenesis and adulthood.
- **Dr Helen Blair** has produced antibodies against EVC and EVC2. She is presently investigating the sub-cellular localisation of EVC and EVC2 in normal and patient cells.
- **Dr Stuart Tompson** has identified protein-protein interacting partners for EVC in two yeast two hybrid screens. He is currently confirming these findings by independent methods.

NEWSFLASH

Members of ESDN have recently published a series of complimentary articles, which describe recent studies focused on pseudoachondroplasia and multiple epiphyseal dysplasia.

- **A recurrent R718W mutation in COMP results in multiple epiphyseal dysplasia with mild myopathy: clinical and pathogenetic overlap with collagen IX mutations.** E Jakkula, J Lohiniva, A Capone, L Bonafe, M Marti, V Schuster, A Giedion, G Eich, E Boltshauser, L Ala-Kokko, and A Superti-Furga. J Med Genet 2003;**40**: 942-948.
- **Missense mutations in the β-strands of the single A-domain of matrilin-3 result in multiple epiphyseal dysplasia.** Gail Jackson, Faye Barker, Eveliina Jakkula, Malwina Czarney-Ratajczak, Outi Makitie, William Cole, Michael Wright, Sarah Smithson, Mohnish Suri, Piotr Rogala, Geert Mortier, Clair Baldock, Andrew Wallace, Robert Elles, Leena Ala-Kokko, and Michael Briggs. J Med Genet 2004;**41**: 52-59.
- **Clinical and radiographic findings in multiple epiphyseal dysplasia caused by MATN3 mutations: Description of 12 patients.** Outi Mäkitie, Geert R. Mortier, Malwina Czarny-Ratajczak, Michael J. Wright, Mohnish Suri, Piotr Rogala, Margarida Freund, Gail C. Jackson, Eveliina Jakkula, Leena Ala-Kokko, Michael D. Briggs, William G. Cole. A J Med Genet Published Online: 21 Aug 2003.

Announcements

- As part of a collaborative effort **Dr Thomas Hertel** (Odense University Hospital, Denmark: thomas.hertel@ouh.fyns-amt.dk) **Dr. Lars Hagenäs** (Astrid Lindgrens Childrens Hospital, Sweden: lars.hagenas@kbh.ki.se) and **Dr. Ilkka Kaitila** (Helsinki University Hospital, Finland: ilkka.kaitila@hus.fi) are updating the Achondroplasia growth curves made by Dr. Horton some 20 years ago. If you have any information that will help their quest including data on height, sitting height, subischial leg length, armspan and head circumference, this would be very useful to them. Please contact them if you are interested in a collaboration on this project.
- Do you have any announcements for the next ESDN newsletter? If so **Email: info@esdn.org**