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In this issue:

RESEARCH CORNER

EPICURE in CORDIS - Scientists identify mutation linked to common form of epilepsy

On the 15th January 2009, publicity was given to the **EPICURE** project on the CORDIS website, which is the official website of EU DG Research. In fact, substantial financial support for **EPICURE** ('Functional genomics and neurobiology of epilepsy: a basis for new therapeutic strategies') is provided through the 'Life sciences, genomics and biotechnology for health' Thematic area of the Sixth Framework Programme (FP6).

The article referred to the discovery by a team of EU-funded Epicure scientists of a mutation on chromosome 15 which is linked to a common form of epilepsy . The findings, which are to be published in the journal Nature Genetics, add to our understanding of the underlying causes of epilepsy and could eventually lead to the development of new drugs to treat the condition.

The article in Cordis reported that epilepsy is one of the most common diseases of the central nervous system, and affects up to 30 million people worldwide. Around half of all epilepsy patients or affecteds have a strong genetic component, and so far about 20 genes linked to the condition have been discovered. However, these genes are linked to very rare forms of epilepsy, and the genetic risk factors behind more common forms of the disease remain unknown.

This study focused on idiopathic generalised epilepsy (IGE), which accounts for one third of all epilepsies. Common IGE syndromes have a predominant genetic aetiology and offer excellent prospects for molecular genetic studies. The scientists studied the DNA of over 1,000 people with IGE and compared it to the DNA of over 3,500 people without the condition.

The researchers found that a small segment in the chromosomal region 15q13.3 was missing in 1% of the IGE patients. None of the healthy people tested had this microdeletion. Previous research has linked the same microdeletion on 15q13.3 to intellectual disabilities, schizophrenia and other neuropsychiatric conditions.

Further research on the patients with the 15q13.3 microdeletion revealed that some had inherited the microdeletion from their parents, while in others the microdeletion appears to have arisen spontaneously. One of the mothers who also had the deletion suffered from panic disorder. However, other parents transmitting to the microdeletion appeared to have no symptoms.

The deleted segment spans about 1.5 Million base pairs and contains at least seven genes, including the CHRNA7 gene coding for the α7-subunit of the nicotinergic acetylcholine receptor. CHRNA7 regulates signalling between nerve cells, and mutations in related genes have been linked to epilepsy in previous research.

These new findings add considerably to our knowledge of the molecular mechanisms involved in both epilepsy and the other neuropsychiatric disorders linked to this microdeletion. With regard to the remarkable phenotypic variability related to this microdeletion, it is difficult to assess its clinical relevance and implications for genetic counseling. Further studies are clearly needed to identify those genetic and environmental factors that contribute to the individual disease phenotype.

Nevertheless, the **EPICURE researchers** are optimistic that their work will eventually lead to the development of new treatments for epilepsy. In the meantime, the **EPICURE** researchers have extended their initial findings implicating that structural genomic variations play a significant role in epileptogenesis. In collaboration with an Australian research group, the association of the 15q13.3 microdeletion with IGE has been confirmed.

Moreover, two additional recurrent microdeletions on chromosome 15q11.2 and 16p13.11 were found to be associated with IGE. Although these recurrent microdeletions are individually rare (<1%) in patients with IGE, they collectively seem to account for a significant fraction of the genetic variance of common IGE syndromes. However,, more research is needed to unravel the complex genetics behind this neurological disorder.

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LATEST NEWS

EPICURE ANNUAL MEETING IN BERLIN

From 6th to 7th February 2009 at Charité Universitaetsmedizin in Berlin, **the THIRD ANNUAL EPICURE PROJECT MEETING** took place. It gathered all 30 partners from 13 European countries. The main aim of the meeting was to discuss management issues and co-ordinate a strategy for dissemination of the project's results. Research work undertaken during the two years of the project was presented and analyzed and the **EPICURE** Partners decided on the activities to be undertaken in the next years of the project.
During the meeting, the project coordinator Prof. Giuliano Avanzini (CO1 INNCB) presented the first version of the second periodic report, drafted with the support of CR29 CFc.
A **HAND-ON COURSE** on the use of new technologies in animal models was organized for the yearly **EPICURE** meeting in February 2009. The Course was organized by **Uwe Heinemann** (CR8 Charité) with the collaboration of **Marco de Curtis** (CO1 INNCB) and took place from February 8th – 14th 2009, just after the **EPICURE** meeting, at the Institute of Neurophysiology Charité Universitätsmedizin in Berlin. The Course was open for max 40 students and young postdocs involved in research for the **EPICURE** projects in Europe. Teachers and tutors of the Course were selected among the **EPICURE** Partners and from the staff personnel at the Institute of Neurophysiology Charité Universitätsmedizin in Berlin. The program of the Course was developed during an ad-hoc meeting in July 2008. After a one-day lecture program the participants of the course familiarized themselves with the facilities in the local laboratories as well as several aspects of experimental epilepsy research. Following demonstration sessions in the morning, the students carried out their own experiments in the afternoon sessions as a mini-project, supported by instructors and tutors, who are EPICURE partners as well as other tutors from the host organization. Additionally, two plenary lectures were given every day.

MEETINGS AND EVENTS

28TH INTERNATIONAL EPILEPSY CONGRESS

The 28th International Epilepsy Congress was held in Budapest from 26th June to 2nd July 2009. It was organised jointly by the International League Against Epilepsy (ILAE) and the International Bureau of Epilepsy (IBE). Over three thousand delegates attended the meeting from more than 80 countries world wide. One of the special event at the congress was the centenary celebrations of ILAE, which was founded in Budapest in 1909... During the congress the most recent scientific and medical developments in its treatment and management were discussed and several **papers from the EPICURE consortium** formed part of the official sessions and programme. IBE organised talks of direct relevance to persons with epilepsy and their families. Issues such as youth, treatment, doctor/patient relationships, campaigns and cross cultural difficulties were discussed. IBE President Susanne Lund spoke about the EPICURE project in her speech at the Opening Ceremony and the initiative was also reported on at its General Assembly. In addition, IBE had produced an information flyer on EPICURE, which was included in the delegate bag of each participant to the congress. The flyers were also available on the Information Stand of IBE in the Exhibition Area.

The Scientific Programme focussed on the following topics:

- Autonomic Functions and Biorhythmicity
- Searching for a Cure – Experimental Models and Human Epilepsy
- Comprehensive Care around the World
- The Family and Epilepsy – Clinical and Social Dimensions
- Brain Development, Plasticity and Epilepsy
- Imaging Epilepsy Networks and Cortical Dysplasia

During this conference the newly elected Executive Committees of ILAE and IBE for the term 2009-2013 began their terms of office.

The next **29th International Epilepsy Congress** will be held in 2011 in Rome and will celebrate the Golden Jubilee of IBE, which was founded in the city of Rome in 1961.

MISCELLANEOUS

RESEARCH PRIORITIES IN EPILEPSY FOR THE NEXT DECADE - A REPRESENTATIVE VIEW OF THE EUROPEAN SCIENTIFIC COMMUNITY

Several funding initiatives are being taken at European Level, using various EU funded research programmes in order to improve the health of European citizens. To date, unfortunately none of the work programmes that specify the research priority areas in FP7 has targeted epilepsy. The Commission on European Affairs of the International League Against Epilepsy (ILAE) has thus undertaken an action in favour of **Epilepsy research**. A Task Force met in Brussels on 17–18 January 2008 and, as a result, published a paper in EPILEPSIA, that is a representative view of the European scientific community on research priorities that should be undertaken in epilepsy for the next decade. This document has been designed in a way that it can be used even by lay persons, at both the national and central levels, for lobbying purposes. It mentions **EPICURE** as a powerful network for the recruitment of large cohorts of subjects for specific types of epilepsy to perform the first genome-wide and large-scale single gene studies and to determine the functional consequences of some selected genetic variants.