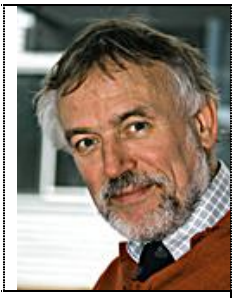
SYSCILIA Newsletter 2 – July 2011

Scientific Advisory Board:

We are happy and proud to announce that the SAB is installed. It consists of four independent scientists who will give critical input to our consortium:

Prof. Veronica van Heyningnen Medical and Developmental Genetics		**Prof. Dr. Alfred Wittinghofer**	
Medical Research Council Human Genetics Unit Western General Hospital Edinburgh		Max Planck Institute of Molecular Physiology Emeritus Group Dortmund Germany	
Research Areas Identifying human disease genes and mutations can reveal how normal biology works and also how it can go wrong in disease. Because many genes and their functions are strongly conserved during evolution, it is possible to use a variety of model organisms including mice, fish and even flies, to study how genes work and interact. Often mutations similar to those that cause disease can be recreated in the model system and studied in great detail, when human patients cannot be studied in the same way. Conversely, there are some non-invasive functional studies in humans that provide information not available from model organisms (eg detailed eye tests, speech and hearing studies, and magnetic resonance imaging). We have identified several genes that lead to overlapping patterns of developmental eye abnormalities, when mutated. Not surprisingly these genes work together in the same pathways. From the different types of mutations, and model organism experiments, we are learning a lot about how developmental regulator genes work and how their expression is fine-tuned. Through hypothesis-driven studies in zebrafish, we are also exploring how environmental factors may interact with mutant genes to alter the outcome of genetic disease		**Research Areas** In the group we are studying various aspects of the biochemistry and structure-function analysis of small and large GTP-binding proteins. We are applying biophysical and biochemical methods such as NMR, fluorescence and X-Ray crystallography to study the interaction of our favorite proteins with its regulators and effectors, both in vitro and if possible, in vivo. A number of these proteins are involved in diseases such as cancer, Noonan and CFC syndrome, neurofibromatosis, tuberous sclerosis, Parkinson and Retinitis pigmentosa.	

Prof. Martijn Breuning
clinical geneticist

Leiden University Medical Center
Leiden
The Netherlands

Research Areas

Clinical Genetics as a part of the Centre for Human and Clinical Genetics underlines the research goal of this centre which is: "To elucidate the molecular and clinical etiology of hereditary disease, congenital malformation, multifactorial disorders and hereditary cancer, in order to improve diagnostics, assist counseling, develop treatments and further prevention."
Area of interest(s):
Mental retardation, congenital malformation, hereditary diseases of the heart, the kidney, and the eye; disorders of growth; genetic counseling; prenatal screening and diagnosis

Prof. Dr. Erich E. Wanker
Proteomics and Molecular Mechanisms of Neurodegenerative Diseases

Max Delbrueck Center for Molecular Medicine
Berlin-Buch
Germany

Research Areas

Millions of people worldwide suffer from neurodegenerative disorders. Most of these illnesses manifest themselves later in life. Therefore, correlated to the increase in life-expectancy the number of people affected with these diseases will grow.

The main objective of our work is to understand the pathomechanisms of late onset neurodegenerative disorders such as Huntington's, Parkinson's, Alzheimer's and Machado Joseph disease and to develop causal therapies for them. The disease causing proteins of these illnesses have been identified, but their functions in the unaffected organism are mostly unknown.
Since the identification of interacting proteins can give clues about the normal cellular function of proteins, we use high-throughput functional genomic approaches for establishing large protein-protein networks.
In vitro and *in vivo* functional assays are developed for high-throughput drug screenings.

Publications and Press releases

New genes for rare inherited diseases discovered

Studying ciliary diseases with proteomics and systems biology techniques led to the discovery of two new genes that play a role in the development of hereditary renal diseases. **Giles** and colleagues studied 850 proteins likely to be involved in three genetic ciliary diseases (Nephronophthisis, Joubert syndrome and Meckel-Gruber syndrome). They have mapped how these proteins interact to predict which of them play a crucial role in the diseases. This led to two genes (Atxn10 and Tctn2) and further research showed that patients indeed carried pathogenic variants of these genes. Sang et al., Cell. 2011 May 13;145(4):513-28.

Disruption of intraflagellar protein transport in photoreceptor cilia is associated with childhood blindness
SYSCILIA researchers have discovered that a specific kind of very early-onset childhood blindness, Leber congenital amaurosis (LCA), can be caused by disruption of the protein transport machinery in the photoreceptor cells of the retina. By using a new quantitative affinity proteomics approach, they were able to identify which exact part of this mechanism was disrupted in patients that suffer from this inherited disease. This study was recently published in the Journal of Clinical Investigation 2011;121(6):2169–2180.

Therapeutic approach for human Usher syndrome: Small molecules ignore stop signals
Usher's syndrome, with an incidence of 1:6,000, is the most common form of congenital deaf-blindness. It is a recessive inherited disease that is clinically and genetically heterogeneous. For sufferers this disease means a major limitation. The hearing loss can be compensated with hearing aids and cochlear implants, but there is still no treatment for the eye. In Hum Gene Ther. 2011 May;22(5):537-47. Epub 2011 Mar 25, researchers from the **Wolfrum** lab showed that a small molecule called PTC124 (ataluren ®), triggers the readthrough of the stop signal in the mutated gene and thus USH1C continues protein synthesis and the functional gene product is produced. Its high readthrough efficiency in combination with excellent biocompatibility makes PTC124 a promising therapeutic agent for PTCs in USH1C, as well as other ocular and nonocular genetic diseases.

Collaborative effort for high impact paper:
Wednesday session at annual meeting in Mallorca: From the ideas and input for a high impact paper the outline generated by the group Nico Katsanis will be send around to all PIs to contribute data if available and applicable.

Annual report.

The Annual Report was submitted to the European Commission by **July 28, 2011**.
The publishable summary can be found on our website. To see the whole report, please login to the wiki page Reporting.

2nd Annual Meeting

The **SYSCILIA 2nd Annual meeting** is scheduled for **May 14, 15 & 16, 2012, London.**
It will be connected with the first European Cilia Conference, to be organized by Phil Beales.

Sessions:

- Clinical Aspects of Ciliopathies
- Structure and Function of Cilia
- Cilia & Development
- Cilia & Disease - human molecular genetics and animal models of ciliopathies
- Translational Therapy and Ciliotherapeutics

Confirmed speakers:

- John Wallingford
- Heymut Omran
- Greg Pazour
- Enza Maria Valente
- Peter Jackson
- Jeremy Reiter

Conference website: cilia2012.org

Mid term review

In addition, the organization of a mid term review will be arranged for the end of June 2012. The aim of this technical review by independent experts is to assess the work carried out under the project and provide recommendations to the European Commission.
All Workpackage Leaders need to participate. Suggested location: Heidelberg.

Calendar 2011

Webinars, online training sessions for the SYSCILIA database, will be planned regularly. These trainings are available for every participant, see the SYSCILIA private website.

The organization of Component Meetings and a Steering Committee Meeting will be planned in the second half of August.

28 Aug – 1 Sept, Heidelberg/Mannheim, Germany:
The 12th International Conference on Systems Biology

For the month November or December 2011, a training will be organized in Heidelberg to discuss and apply the data sharing and exchange and the use of the central database.

Website

Now available on the website two new pages, 'Links' and 'Jobs'.
As SYSCILIA member you can post new jobs and/or links on these pages. The pages are visible to everyone.

Congratulations:

On the 1st of April **Hannie Kremer**, RUNMC - partner 1b, has been appointed to Professor of Molecular Otogenetics.

The **International Four Day Marches Nijmegen** (or **Vierdaagse**) is the largest marching event in the world. It is organised every year in Nijmegen in mid-July as a means of promoting sport and exercise. The 95th edition is behind us. On Friday 22 July, 38,422 participants were cheered on while walking over the Via Gladiola to the finish to receive their well-deserved medal. SYSCILIA's coordinator, Ronald Roepman, was one of them. He walked four days in a row, 50 km per day and was awarded with the royally approved medal "Cross for demonstrated marching skill".