The 5th International Symposium of the Lowe Syndrome Trust
'Molecular and Clinical Advances in Lowe Syndrome'
Royal Society, London, 12th December, 2014
hosted by Penny Lancaster Stewart

The 5th International Lowe Syndrome Trust Symposium was held, as in previous years, at the prestigious location of the Royal Society in Pall Mall, London. This year, the scientific programme was followed by a drinks reception and poster session, allowing the scientists studying Lowe syndrome to meet with potential sponsors and other interested parties. This session was vibrant and an excellent way to conclude the symposium.

The scientific programme covered various aspects of Lowe syndrome and the related Dent disease, and there were also excellent presentations on how cutting edge stem cell technology may be applied to rare diseases such as Lowe Syndrome and Dent Disease.

The first two talks were by **Robert Nussbaum** (UCSF) and **Martin Lowe** (University of Manchester), who described mouse and zebrafish animal models to study Lowe syndrome. It is apparent that such models will be invaluable in deciphering disease mechanisms as well as for testing potential therapeutic compounds. Related to this, in his talk **Rudiger Woscholski** Imperial College London) described how he is developing a novel lipid-sequestering molecule to counteract some of the features of Lowe syndrome. This novel approach will hopefully lead eventually to a treatment for Lowe Syndrome. Similarly, **Claudio Aguilar** (Purdue University) explained that he has identified two compounds, already with FDA approval, that are effective in correcting some of the defects seen in cultured Lowe syndrome cells. The next step will be to test these compounds in more physiological model systems, such as the zebrafish model described by Martin Lowe and others, to test their efficacy in correcting Lowe syndrome phenotypes. The drug screening approach is also being used by **Antonella De Matteis** (TIGEM Institute Naples) who described how her laboratory has identified a number of compounds that are able to correct defects seen in Lowe syndrome cells in culture. Again, it will be interesting to see what these compounds do in animal models of Lowe syndrome.

Detlef Bockenhauer (UCL London) described a renal Fanconi syndrome (with some, but not all, of the renal features of Lowe syndrome) caused by an unusual mistargeting of a peroxisomal protein to the mitochondrion, resulting in impaired mitochondrial function, reduced energy production and, consequently, a renal uptake defect (renal uptake is a very energy consuming process). It was also speculated that mitochondrial dysfunction may contribute to Lowe syndrome, as had been suggested previously.

Three talks presented recent data on the cellular functions of the Lowe syndrome protein OCRL1. **Ramiro Nandez** from the De Camilli laboratory (Yale University) described a role for OCRL1 in clathrin-mediated vesicle traffic, while **Antonella De Matteis** described a novel role for the protein in lysosomal function. **Laura Swan** (University of Liverpool) described the recent progress she has made in studying OCRL1 in slime mould, an excellent genetic model, giving new insights into the evolutionarily conserved functions of this protein.

After lunch, the eminent guest speakers **Bruce Conklin** (UCSF) and **Juan Carlos Izpisua Belmonte** (Salk Institute) described how cutting edge stem cell technologies are being used for the study and potential treatment of rare genetic disorders such as Lowe syndrome. These rapidly evolving technologies offer great potential and could revolutionize the way genetic disorders are treated in future.

The final session concentrated on the nervous system and the neurological aspects of Lowe syndrome. **Chris Oliver** and **Jane Waite** (University of Birmingham) described the distinctive behavioural features of Lowe syndrome and how a better understanding of these can help improve the support offered to Lowe syndrome patients. **Mercedes Serrano** (Hospital Sant de Deu, Barcelona) continued on this theme by describing attempts to better define the neurological phenotype of Lowe Syndrome patients. The next two talks, which concluded the scientific programme, focussed on the cellular defects that occur within the nervous system with loss of OCRL1. **Nael Nadif-Kasri** (Department of Human Genetics Nijmegen) described how impairment of OCRL1 leads to vesicle trafficking defects in neurons. **Sean Sweeney** (University of York) described a novel fly model for Lowe syndrome that has a strong neurological phenotype, which again could arise from vesicle trafficking defects within neurons. Further studies will be required to decipher precisely how such defects at the level of neurons relate to the neurological symptoms seen in Lowe syndrome patients.

It was clear from the varied presentations that immense progress has and continues to be made in our understanding of Lowe syndrome. Not only that, but our improved understanding is now leading to the search for potential therapeutics, with several candidate molecules already undergoing testing in various experimental models. The obvious hope will be to translate this work into human patients at some point in the future. This rapid progress is in no small measure down to the funding provided by the **Lowe Syndrome Trust** in the UK and should be acknowledged not only for its outstanding efforts in supporting scientific research, but also for the support it provides for Lowe syndrome patients and their families.

" Fantastic science, some on Nobel prize level. It was a privilege to have been part of it"

Dr Detlef Bockenhauer

"Thank you so much for such a fantastic symposium... it allowed me to establish possible collaborations with other scientists and doctors trying to advance research"

Professor Juan Carlos Izpisua Belmonte

The Lowe Syndrome Trust

www.lowetrust.com

"Thank you for hosting such a terrific meeting. I was very impressed by the progress you have made in a short time"

Professor Bruce Conklin

"Thank you to the Lowe Syndrome Trust for organising another high-quality scientific meeting. I am particularly pleased about the advance in research fostered by the Trust, with most talks clearly pointing out the opportunities to screen for potential drugs to remedy the symptoms of Lowe Syndrome. The LST's impact goes well beyond the monetary value of the raised funds for research, with many scientific careers and outputs now being influenced by the Trust's funding and visibility. Since the LST came into being we have seen a doubling in publications that are addressing the target protein of Lowe syndrome, OCRL; this achievement is certainly due to your effort and determination in setting-up and establishing the top research-focussed charity on Lowe syndrome and Dent's disease. I think you can be proud of what you have achieved" ***Dr Rudiger Woscholski***