The Lowe Syndrome Trust

THE LOWE SYNDROME TRUST UK - NEWSLETTER SEPTEMBER 2023

After the Covid freeze, we are now resuming activities and fundraising, starting with confirming all our charity patrons, supporters and families. The main activities and news is listed below.

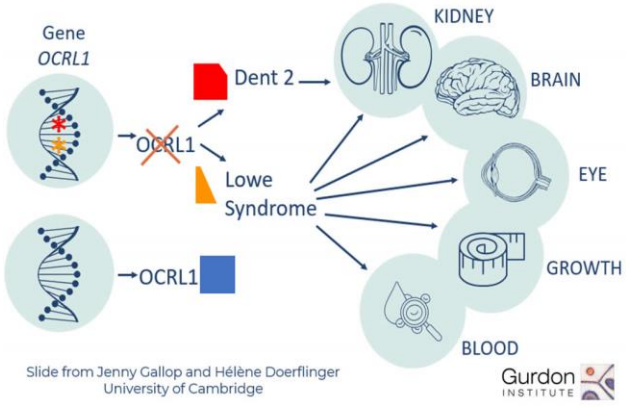
March 2023 - LST charity visit to The Gurdon Institute, University of Cambridge and new Lowe medical board member Jenny Gallop

in March 2023 CEO Andrew Thomas and son Oscar visited the Gallop lab to share experiences, discuss recent drug discoveries and working together to promote research. We are delighted to announce that Dr Jenny Gallop has agreed to become a member of the LST medical board. Jenny's team have produced a short video on potential treatments for Lowe condition with Alpelisib see: https://youtu.be/A8pOk3pVF4k?si=uoiHnEBgGHCENE31

LST participation with Cerebra Neurological survey

The Cerebra Network for Neurodevelopmental Disorders is a collaborative research network, working across the UK at the University of Birmingham, Aston University, University of Surrey, and University of Warwick – you can find out more about the team at www.cerebranetwork.com.

The LST will be reaching out to families to participate in the BEOND that is an ambitious survey exploring wellbeing, behavior, sleep, health, emotion, and development in people with a variety of genetic syndromes, intellectual disability, and neurodevelopmental disorders**.** You can find out more about the survey here: https://www.cerebranetwork.com/beond-lowe



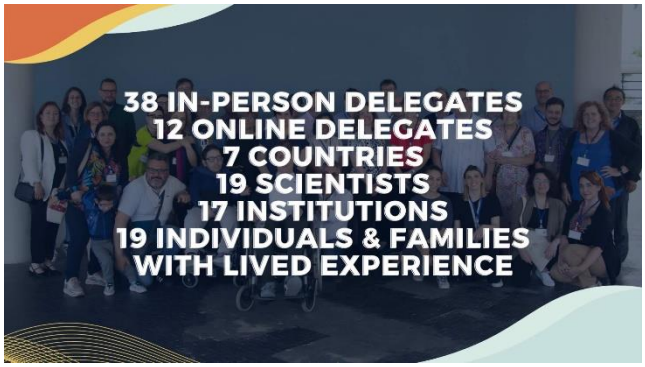
One of our goals in this study is to be able to look at changes over time to better understand development across the lifespan in Lowe syndrome. If you are happy for us to link your responses in this survey to data we may have collected from you in the past then you will be asked at some point to enter a historical Cerebra participant ID.

DNA tests and NHS genetic services for Lowe Syndrome

NHS England has announced new genetics analysis services, genetics database, support for patients with learning difficulties and at-home blood and kidney monitoring services. Please

see the charity webpage we created and please contact Anna@lowetrust.com for comments and feedback. Please see webpage https://www.lowetrust.com/families/ **Private DNA tests**. A DNA test for Lowe Syndrome requires whole Genome Sequencing and this can be provided on the NHS by a GP request to your local hospital genetics specialist reference test R31 bllateral cataracts. There are also a number of private DNA genetics services confirmed by the charity to provide Lowe Syndrome tests and consultations for ~ UKP 500, an example being Dantelabs https://www.dantelabs.com/products/rare-disease-health-package

May 2023 Lowe Syndrome Medical Research Summit in Naples



The International Lowe Syndrome medical conference was held at the Telethon Institute of Genetics and Medicine (TIGEM) in Pozzuoli, Naples, Italy 24th-25th May 2023 in partnership with the Lowe Syndrome Trust, the Gurdon Institute Dr Jenny Gallop lab, TIGEM, the LSA USA and others.

The conference brought together scientific and medical professionals, stakeholders and families to present and discuss basic and translational research activities going on worldwide to improve the knowledge of cellular roles of OCRL, to present new models to study Lowe syndrome and to accelerate the progress towards treatments or other therapeutic options for patients with Lowe Syndrome/Dent2 disease.

LST CEO Andrew Thomas, Trustee Dr Joseph Laycock and spokesperson Paul James were delighted to participate in the conference and to meet with Jeri Kubicki, president Lowe Syndrome Association, USA and AISLO Italy, families and researchers.

The conclusion from the conference was that all participants agreed to work closely together and have a common process for research grant applications, joint funding and strategy to support a global patient registry and potential clinical trials. There were a number of families at the conference and LST spokesperson Paul James who has the condition presented at the conference on what it's like to have the condition and to refer to Lowe as having a condition rather than a disease.

The agenda and slides on the presentations at the conference can be found here www.lowemeeting2023.org

http://lowemeeting2023.org/Final_program.pdf

http://lowemeeting2023.org/Final_Abstract_Book_English.pdf

Lowe Syndrome Science Presentation Summaries

New Charity Patrons

We are delighted to have new Patrons - England cricketer Graeme Swann and social influencers Oliver Evans and Mark Emms. For cricket fans Graeme needs no introduction. Graeme is charity spokesperson Paul James Brother-in-law and Oliver, founder of The Kin is a cousin of Oscar Thomas who has Lowe condition. Mark Emms and Oliver have supported the charity organizing charity balls and inviting celebrity's.

New Trustee

I would like to Welcome patron Mike Fennings to the board of trustees**.** Mike has agreed to step up to the board having been a long-standing supporter and fundraiser for the charity and family having organised the infamous cycle tours.

Potential pilot clinical trials drug therapies Alpelisib and Piclidenoson.

Helped by the Lowe Syndrome charity funding of medical research projects, the links between the OCRL1 genetic mutation, cell biology and symptoms are better understood and a number of drugs have been identified to treat Lowe and Dents-2 syndrome.

These are already FDA approved drugs prescribed for conditions such as breast cancer and psoriasis and pilot clinical trials are being proposed to treat Lowe Syndrome.

To do this we are reaching out to UK families to use the recently announced NHS genetics and health monitoring services to identify the genetic mutation and monitor kidney function. Please see NHS and GP services article on the charity website https://www.lowetrust.com/families/

There two drugs currently under consideration for pilot clinical trials - Alpelisib and Piclidenoson.

Alpelisib

Researchers at the universities of Cambridge and Zurich have found that drug Alpelisib newly approved for cancer, improves kidney dysfunction in a mouse model of Dent disease 2 and Lowe syndrome. The study offers hope for the first disease-modifying treatment. In addition to kidney dysfunction, characteristic of Dent disease 2, boys with Lowe syndrome also require eye cataract surgery as newborns and suffer seizures and other disabilities.

Only supportive treatments are available, such as nutrient supplements and help with learning.

These rare conditions are caused by the lack of an enzyme called OCRL that normally controls the lipid composition of cell membranes. The disruption activates a system of filaments inside the cells, called the actin cytoskeleton, in the wrong place. The actin blockage means that the cells in the kidneys that usually reabsorb filtered proteins and essential nutrients don't work properly, causing a loss of these in the urine.

Dr Jennifer Gallop's group at the Wellcome Trust/ Cancer Research UK Gurdon Institute in Cambridge worked out how the actin system was being activated by the disruption in cell membrane lipids. "By understanding the details of what is happening in cells during Lowe syndrome and Dent disease 2," said Dr Gallop, "we realised that alpelisib, a drug that is already approved for use in patients with cancer, could prevent the actin blockage." This is because alpelisib targets a different step in the pathway, and rebalances the lipid composition.

The Gallop group teamed up with Professor Oliver Devuyst from the Institute of Physiology, University of Zurich to test alpelisib in a humanised mouse model of Lowe syndrome and Dent disease 2. Devuyst said: "Amazingly, treatment with alpelisib improved the actin cytoskeleton of the kidney cells and rescued the reabsorption of the filtered proteins."

The researchers don't yet know whether the drug will work in patients and if their neurological symptoms will be helped as well. However, because alpelisib has been used before in another rare disease in children, as well as in adults, there is evidence that it is safe. These efforts of repurposing a drug could potentially lead to the cost- effective development of a treatment for these rare disorders

A press release announcement from the Gurdon Institute Cambridge on Alpelisib can be read here https://www.businessweekly.co.uk/news/academia-research/cancer-drug-can-rebalance-kidney-function-devastating-genetic-disease

Piclidenoson

Biotechnology company Can-Fight BioPharma Ltd plans to develop Piclidenoson for the treatment of Lowe Syndrome, based on research by Dr. Antonella De Matteis, Professor of Biology, Department of Molecular Medicine and Medical Biotechnology at the University of Naples Federico II, and Program Coordinator of the Cell Biology and Disease Mechanisms at The Telethon Institute of Genetics and Medicine (TIGEM) in Italy.

"Having tested thousands of compounds in search of a treatment for Lowe Syndrome, Piclidenoson is the only compound we've found to date that has shown to be effective in preclinical studies. Importantly, we observed that Piclidenoson treatment in mouse models of Lowe syndrome leads to a significant decrease of the urinary loss of proteins in diseased animals," Dr. De Matteis stated. "We chose to investigate Piclidenoson based on the availability of extensive scientific data showing its excellent safety, coupled with efficacy in this disease which involves renal, cerebral, and ocular manifestations."

Can-Fite Chairman Dr. Pnina Fishman commented, “We are hopeful that Piclidenoson can offer a much needed treatment for infants, children, and young people living with Lowe Syndrome. Based on Piclidenoson’s proven safety profile in clinical trials to date, and because Lowe is a rare disease in dire need of treatment, we plan to move into an advanced stage clinical study which may open a path to approval. Dr. De Matteis and her team have made an impactful discovery with Piclidenoson and we look forward to working with her and Fondazione Telethon.”

A press release announcement can be found here:
https://www.businesswire.com/news/home/20230824833299/en/

Fundraising
To save costs we are closing the physical office in Finchley Road, and going virtual and digital. The website is being updated and will be the platform for all information. The office address 673 Finchley Road, London NW2 6JP can continue to be used for mail.

The big lottery community grant has been resumed and this is limited to funding an outreach program to contact up to 50 Lowe families, including visiting the family and assisting with NHS services, social services and benefits. The funding also for an update of the charity communications and to produce a guide to UK Adult care to help families plan for the future adult care, including legal and government benefit entitlement, social services assessments, placement in suitable residential care and assisted employment

It is also hoped that a number of families can be identified for potential clinical trials for the recently announced drug therapies.

We have received applications for research grants, and a proposal for pilot clinical trials so we urgently need to fundraise. We will be writing and applying to our previous donors to plead for funds to support charity running costs, ongoing research for example Purdue and we have set aside £20000 for potential pilot clinical trials. Also the next Lowe medical research conference is being planned with Perdue USA that will need funds.

Family Fundraising - Gofundme
We have families and supporters fundraising, Paul James raised over £1000 for his Naples and walking for Lowe fundraiser. **Catherine Taggart** is doing the AJ Bell Great Scottish run half marathon in October - see GoFundMe, https://gofund.me/52fe76f7

Lowe Syndrome meeting for local families and lab visit Nov 12-14th Cambridge
We are planning another visit to the Janny Gallop Lab in Cambridge and family outreach meeting for families wishing to meet, the charity will expense travel and overnight sray, please register with anna@lowetrust.com for attendance.

For charity volunteers please take a look at the charity overview slides, and the org chart and feedback any comments https://www.lowetrust.com/wp-content/uploads/2023/07/Lowe-Sydrome-Trust-Presentation-2023.pdf

Many thanks for your support

Yours sincerely

Andrew Thomas
CEO The Lowe Syndrome Trust
www.lowetrust.com