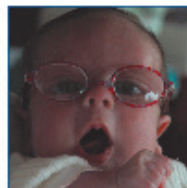
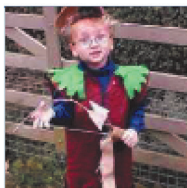


The story so far...



Care today... cure tomorrow



Lowe Syndrome Trust

www.lowetrust.com

Registered Charity #1081241



I am very proud to be part of such a small, tremendous charity. Lowe syndrome is a devastating incurable children's disease, affecting the brain, eyes, kidneys, bones and muscles, sadly leading to a short life expectancy. The Lowe Syndrome Trust is the only UK charity for the disease, and by encouraging scientific discovery we are committed to improving the outlook for children with Lowe syndrome.

Jonathan Ross, OBE
Trustee of the Lowe Syndrome Trust

I am honoured as a patron to be such a part of this wonderful energetic charity which has achieved amazing results. It strikes a chord that a mother, Lorraine, is actually initiating medical research and fundraising for support.

Penny Lancaster
Patron of the Lowe Syndrome Trust



Although the charity is still very small in the past 19 years we have raised hundreds of thousands of pounds, and in fact we have become the main fundraiser for research into this incurable disease

Tony Hadley
Patron of the Lowe Syndrome Trust

With your help we can continue to support the families affected by Lowe syndrome and work towards finding a cure.

Melanie Sykes
Patron of the Lowe Syndrome Trust



Nineteen years on....

The *Lowe Syndrome Trust* is a UK Charity formed in June 2000 by Lorraine and Andrew Thomas after their son was diagnosed with Lowe syndrome. Lowe Syndrome is a genetic disorder that can occur with no family history, affecting boys with multiple physical and mental handicaps, including cataracts in both eyes, muscle weakness, kidney problems, cysts, brittle bones, arthritis, poor growth, mental impairment with behavioural problems, and epilepsy. Sadly the life expectancy for these children may be short due to the complications of the disease and the lack of funding to find a cure.



In the 19 years since the charity was launched by Jonathan Ross at PJs winebar, the *Lowe Syndrome Trust* has sought to support families affected by Lowe Syndrome as well as help to raise awareness of the disorder and resource

teachers and healthcare professionals. The *Lowe Syndrome Trust* has become the largest source of funding for research into Lowe Syndrome in the world.



Since 2000 there have been some major research breakthroughs in treating Lowe syndrome, leading to improved care and quality of life, but there is still so much to do. With your help and ongoing support we look forward to continuing to improve the quality of life and care for these boys, and one day to find a cure that will release them to live full and happy lives.



This booklet aims to give you a taste of what we have achieved so far and to give you a glimpse of where we are going . . .

About us

What is Lowe Syndrome?

Lowe syndrome is a genetic disorder caused by a missing enzyme, which affects many organ systems, particularly the brain (with seizures, mental retardation, impaired speech and developmental delay), the kidneys (with loss of important salts and nutrients, and eventual kidney failure), the eyes (with cataracts), the bones (with deformity and arthritis), and the muscles (with weakness). Unfortunately, Lowe syndrome boys have a shortened life expectancy.

Trustees

Our board of trustees is made up of people who we trust!

The trustees make sure the *Lowe Syndrome Trust* is running well and is doing what it was set up to do – they are responsible for keeping us moving forward in the right direction. The trustees freely give their time and energy to make sure we spend our funding wisely and stay within the law, and also represent the charity at numerous important events and meetings.



Ms Lorraine Thomas (Chair)



Mr Jonathan Ross OBE

Ms Carolyn Mitchell

Ms Penny Biziou

Dr Joseph Laycock

Contact us

For further information, contact Lorraine Thomas

Tel: 0207 7948858

Email: lowetrust@gmail.com

Mobile: 07958 444020

or visit www.lowetrust.com

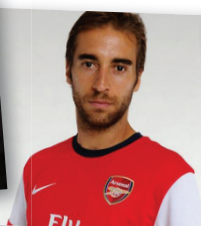
Registered Charity 1081241

Patrons

We are greatly indebted to our many wonderful patrons who support us in our work to find a cure for Lowe Syndrome – none of our achievements would have been possible without their help.



Baroness Susan
Greenfield CBE



Mathieu Flamini



Penny Lancaster



Melanie C



Sir Richard
Sykes



Jonathan Coleman



Melanie Sykes



Christopher Biggins



Melanie Blatt



Tony Hadley



Tom Conti



Tris Payne



Lisa Voice



Richard Desmond



Susie Webb



Seville Bulpitt



Michael Fennings



Mark Emms

Fundraising

Here are a few examples of the ways in which we and our supporters have raised money to support families affected by Lowe syndrome.

- In 2016 LST trustee Jonathan Ross launched a Charitable Bookings promotion so people can donate when booking restaurant tables.
- Also in 2016 we initiated the Lowe Syndrome Legacy Gift scheme. Any gift left in a will, no matter how large or small, will make a lasting difference in the fight against Lowe syndrome.
- The *Lowe Syndrome Trust* was one of *Melanie C*'s nominated charities for her official 2013 calendar.
- Also in 2013 chart-topping pop stars *One Direction* donated a signed hoodie to be auctioned to raise money for the *LST*.
- In 2012 Penny Lancaster Stewart supported the *LST* in the million pound *Garden of Hope* (gardenofhope.co.uk)
- In December 2011 the *LST* were selected as one of the chosen charities for the *ICAP Charity Day* in the City of London.
- In May 2008 we held a Lowe Syndrome Charity Gala Ball featuring Dynamo, Christopher Biggins and Bryan Ferry.
- At the 2008 *Medical Futures Innovations Awards*, we auctioned Jonathan Ross' motor scooter, tickets to the BAFTA awards and a picture donated by Penny Lancaster and Rod Stewart.
- We released a Christmas album, "A Christmas Soul", in 2008, recorded and produced by the AM Band.
- The 2006 annual *Ladies Who Lunch* on behalf of the LST was hosted by Jonathan Ross and Jono Coleman. The raffle included Joss Stone's Skateboard, a signed photo donated by George Michael and Liz Hurley's Versace shoes.
- In 2006 we held a Masquerade Ball, featuring an auction including items donated by Rod Stewart, Shirley Bassey and All Saints.
- Dave Cornthwaite set a world skateboarding distance record in 2006, 3000 miles across Australia raising money for *LST*.



Lowe Family Quotes

The following are quotes from parents of Lowe boys. They highlight just some of the reasons why we need to fund medical research in the hope of better treatments and a cure

"He is still in hospital and actually doing quite well. He is still on the ventilator and they have started weaning him slowly off of it. He isn't seeing right now because of the bleeds he had in his brain in the area that effects sight. They remain hopeful it should return when the bleeds heal. I hope so..."

"These boys have so much fight in them, more than they are given credit for."

"... just undergone 3 surgeries in the left eye and 2 in the right eye. Both eyes now have valves in them to alleviate the pressure. We hope that we have seen the last of the surgeries for some time now. He is a strong boy, much stronger than mum, when it comes to all he has to endure in his daily walk through life."

"Everything in our boys lives are so special. I now know that before he was born I took a lot of things for granted. Now every little accomplishment that he does is a very big thing"

"I love my son more than anything in the world, but I can honestly say I absolutely hate this syndrome with everything in me. It is very ruthless and seems so cruel. We just take things one day at a time..."

"The doctors have told us that he may never sit or walk again because of his muscle weakness. He was on such a high dose of medicines to keep him alive, his muscles shut down on him, and now we have to slowly work them back up. It could take months, it could take years. I don't care though, as long as we can bring him home again. He has now been in the hospital for 3 months. And it seems like 3 years"

"There are babies that started after him and are already crawling and walking and he has not even started to try too much of either yet. We just focus on the wonderful things he can do and all the joy he brings into our life!"

In 2006 he had a hip replacement. Since then he has developed severe epilepsy, can no longer walk, has arthritis, more eye problems, almost died with septicaemia and has a kidney function of 8%. And he still loves every minute of his life and every day is a joy to him!

"Our son, will be 2 years old in 17 days, needs to have surgery to close up a hole in his stomach where the gastrostomy button was. This will be his 10th surgery and putting him under anesthesia just breaks our hearts. He always has a tough time coming around afterwards. Hearing him cry is just enough to make anyone's heart feel very heavy. That is how I am feeling right now, like my heart is being weighed down by a million bricks".

Press

The *Lowe Syndrome Trust* has been featured in numerous press, TV and radio articles. Press articles have appeared in: *OK! Magazine*, *Hello! Magazine*, *Good Housekeeping*, *The Daily Mail*, *The Daily Express*, *The Daily Star*, *Take it Easy*, *Ham & High* and the *Southampton Daily Echo*.

TV features include: *ITN News*, *Grampian News*, *This Morning* and *Channel 5* as well as on *Who Wants To Be A Millionaire?* and *Tipping Point* as the charity nominated by Jonathan Ross, and again on *Who Wants To Be A Millionaire?* nominated by Penny Lancaster. The *LST* has also appeared on the *BBC Radio 4 Appeal*, *You and Yours* and *LBC Radio*.

We have also appeared in internet articles on the BBC News website (news.bbc.co.uk) and Look to the Stars (looktothestars.org).



BBC
RADIO



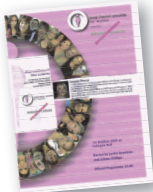
LBC 97.3 FM
London's Biggest Conversation

YOU & YOURS
Weekdays 12 noon
Radio 4's consumer affairs programme



Awards

2016: Lorraine & Andrew Thomas were invited to No. 10 Downing Street to meet with Secretary of State, Karen Bradley for a lunch reception in honour of small voluntary charities such as the Lowe Syndrome Trust.



2009: Lorraine Thomas was nominated for the *Inspiration Awards for Women* in the 'Most Inspirational Non Celebrity' category for her work setting up and running the Lowe Syndrome Trust.

2008: We were invited to attend the *Medical Futures Innovations Award* dinner, where trustees Lorraine Thomas and Jonathan Ross OBE presented the work of the charity.



2005: The *Lowe Syndrome Trust* received a *Charity Award for Online Transparency*, sponsored by CAF (Charities Aid Foundation) and The Institute of Chartered Accountants in England and Wales (ICAEW) and was granted a seal for our website www.lowetrust.com

2004: The Lowe Syndrome Trust received a commendation at the *Charity Finance Magazine Awards*, in the medical and healthcare category. The Charity Awards recognise and celebrate excellence in leadership and management of charities.



2004: The Lowe Syndrome Trust was nominated Grant Thornton Charity of the Year.

2004: Lorraine Thomas was nominated for the *Good Housekeeping Olsen Inspirational Women Award* for her work setting up the the Lowe Syndrome Trust.



Resources

The Lowe Syndrome Trust produce a range of resources to support families affected by Lowe syndrome as well as resources for education and healthcare professionals who care for these boys.

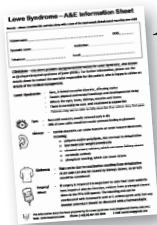
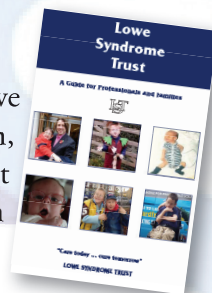


Website - www.lowetrust.com

Our website is the first port of call for many families when they first learn that their son is affected by Lowe syndrome. The site features a wealth of useful information and links and has won an award for online transparency.

Handbook

This is a guide for families and professionals affected by Lowe syndrome, covering many different aspects of the condition, from medical symptoms to behavioural effects, to the latest scientific breakthroughs. This is sent out free and will soon also be available as an eBook and website download.



A&E Information Sheet

We have put together an *A&E Information Sheet* that details the important medical features of Lowe syndrome, which can be printed off and given to aid emergency healthcare workers, who may otherwise be unaware of the symptoms and medical management of Lowe syndrome.

We also send out emergency medical bulletins to families and professionals, for example one concerned the discovery of a platelet disorder in Lowe Syndrome which affects blood clotting and therefore emergency healthcare and surgery.

Newsletter

In addition to the website and booklet, we produce a regular newsletter which is sent out to families and doctors with all the latest updates about Lowe syndrome.



Scientific Advisory Board

One of the major aims of the *Lowe Syndrome Trust* is to raise money to fund medical and scientific research into Lowe Syndrome to better understand the disease, develop treatment and eventually work towards a cure.

In order to use the funding we raise wisely we are ably supported by a board of expert clinicians and scientists, each a world expert in their field.



Mr Nimalan Maruthainar

Consultant Orthopaedic Surgeon, Royal Free Hospital, London



Dr Detlef Bockenhauer

Consultant Nephrologist, Great Ormond Street Hospital, London



Professor Robert Unwin

Professor of Nephrology & Physiology, University College London



Professor Shamshad Cockcroft

Department of Physiology, University College London



Professor Philip Beales

Hon Consultant in Clinical Genetics, Institute of Child Health, London



Dr Rudiger Woscholski

Senior Lecturer, Division of Cell & Molecular Biology, Imperial College London



Professor Helen Cross

Reader, Paediatric Neurologist, Epileptology, Great Ormond Street Hospital, London



Professor Sir Peng Khaw

Professor of Glaucoma and Ocular Healing and Consultant Ophthalmic Surgeon, Institute of Ophthalmology, University College London



Professor Robert Kleta

Potter Chair of Nephrology, Internal Medicine, Royal Free Hospital, London



Dr. Richard Sandford PhD FRCP,

University Reader in Renal Genetics, Honorary Consultant in Medical Genetics, Academic Laboratory of Medical Genetics, University of Cambridge

Scientific Grants

The *Lowe Syndrome Trust* is committed to funding research to find a cure. Through fundraising we have been able to award over 20 major scientific grants to researchers in the UK and USA for projects to better understand what causes Lowe syndrome and to develop new treatments.



- 2002 – £25,000 contributed to three research projects through the LSA
 - Great Ormond Street Children's Hospital
William Van't Hoff, Robert Unwin, Guido Laube – £9,000
 - Imperial College London, Department of Chemistry
Dr Vilar-Compte and Dr Rudiger Woscholski – £50,000
- 2003 – Dundee University, Scotland, *Dr John Lucocq* – £50,000
- 2004 – University College London, *Professor Shamshad Cockcroft* – £50,000
- 2005 – Institute of Ophthalmology (Moorfields), *Dr Tim Levine* – £50,000
 - Addenbrooke's Hospital, Cambridge, *Dr Anthony Norden & Professor Robert Unwin* – £20,000
- 2006 – Institute for Human Genetics and Department of Medicine, University of California, *Professor Robert L Nussbaum* – £102,000
- 2007 – Dundee University, Scotland, *Dr J Lucocq* – £10,000 extension
 - University of Manchester, *Dr Martin Lowe* – £80,000
- 2008 – Purdue University Indiana, *Dr Claudio Aguilar* – £80,000
 - Imperial College London, *Dr Rudiger Woscholski* – £80,000
 - University of California, *Professor Robert Nussbaum* – £61,000 extension
- 2010 – Institute of Ophthalmology (Moorfields), *Dr Tim Levine* – £80,000
 - Yale University, *Professor Pietro De Camilli* – £80,000
 - Manchester University, *Dr Martin Lowe* – £79,000
 - Purdue University/Institute of Child Health UK, *Dr Aguilar & Professor Philip Beales* – £100,000
- 2012 – Manchester University, *Dr Martin Lowe* – £80,612
 - Imperial College London, *Dr Rudiger Woscholski & Ramon Vilar* – £200,000
 - UCL/Royal Free Hospital/Great Ormond Street Children's Hospital, *Professor Kleta, Professor Unwin & Dr Bockenbauer* – £84,000
- 2103 – Manchester University, *Dr Martin Lowe* – £13,000 extension
- 2014 – University of Birmingham, *Professor Chris Oliver* – £67,000
 - Manchester University, *Dr Martin Lowe* – £10,000
- 2015 – Purdue University/Manchester University (joint project)
Professor Martin Lowe & Professor Claudio Aguilar – £50,000
- 2016 – Manchester University, *Prof Martin Lowe* – £60,000
- 2017 – Institute of Genetics & Medicine, Naples, *Prof Antonella De Matteis* – £80,000
 - Manchester University, *Prof Martin Lowe (continuation funding)* – £10,000
- 2019 – Manchester University, *Prof Martin Lowe (continuation funding)* – £25,000

The *Lowe Syndrome Trust* has also funded 6 international Lowe Syndrome symposia: 4 at The Royal Society, London, 1 at the NIH in Bethesda, USA and 1 at The American Cell Biology Conference, San Diego, USA.

Researcher Quotes



"The *Lowe syndrome Trust* has a crucial role to play by raising funds and targeting them towards research in ways that governmental funding is simply not going to do because of the rarity of the disease. We are collaborating in an international effort to find drugs that can reverse the defect in our animal model leading eventually to clinical trials in patients. I could not have done this work without the support of the Trust"

Professor Robert Nussbaum – *University of California* **UCSF**



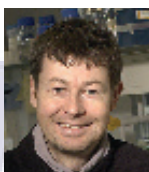
"The *Lowe Syndrome Trust* has made an enormous contribution – not only in raising awareness and providing support for patients and families, but also in having a very strong impetus to research, both in funding and in encouraging collaborations through international scientific symposia.

Professor Robert Unwin – *Chair, Lowe Scientific Advisory Board*



"The *Lowe Syndrome Trust* has been key to our studies on the structure, properties and biological functions of OCRL, the protein encoded by the Lowe syndrome gene. Equally important have been the workshops sponsored by the *Lowe Syndrome Trust*."

Pietro De Camilli – *Yale University* **Yale SCHOOL OF MEDICINE**



"My laboratory has received five research grants from the *Lowe Syndrome Trust* which have proved instrumental in developing a zebrafish-based model. We hope to develop a screen for compounds to treat the condition. Without the funding of the LST this would just not be possible."

Dr Martin Lowe - *Manchester University* **MANCHESTER**
The University of Manchester



"Thanks to funds from the *Lowe Syndrome Trust* our lab discovered evidence connecting Lowe syndrome to other developmental diseases. This is important because breakthrough in new therapies for other diseases could be immediately capitalised on by researchers working on Lowe syndrome."

R Claudio Aguilar – *Purdue University* **PURDUE**
UNIVERSITY



"Funds from the *Lowe Syndrome Trust* have made all the difference to our knowledge of this rare but devastating disease. We have discovered that the disease affects the way cells grow in contact with their neighbours, which is crucial in the major organs affected in the disease: the eye, brain and kidney."

Dr Tim Levine – *Institute of Ophthalmology, London* **UCL**

Scientific Publications

Research papers

The research we have funded has led to the publication of at least 20 scientific research papers. These papers allow the researchers we fund to share findings with the international scientific community to work together towards new treatments and eventually find a cure.

Early proximal tubular dysfunction in Lowe's syndrome. Laube GF, Russell-Eggitt IM, van't Hoff WG Arch Dis Child. 2004 89:479-80

Renal phenotype in Lowe Syndrome: a selective proximal tubular dysfunction. Bockenhauer D, Bokenkamp A, van't Hoff W, Levchenko E, Kist-van Holthe JE, et al. Clin J Am Soc Nephrol. 2008 3:1430-1436

Lowe syndrome patient fibroblasts display Ocr1-specific cell migration defects that cannot be rescued by the homologous Inpp5b phosphatase. Coon BG, Mukherjee D, Hanna CB, Riese DJ 2nd, Lowe M, Aguilar RC. Hum Mol Genet. 2009 18:4478-91

Species-specific difference in expression and splice-site choice in Inpp5b, an inositol polyphosphate 5-phosphatase paralogous to the enzyme deficient in Lowe Syndrome. Bothwell SP, Farber LW, Hoagland A, Nussbaum RL Mamm Genome. 2010 21:458-66

Mouse Model for Lowe Syndrome/Dent Disease 2 Renal Tubulopathy. Bothwell SP, Chan E, Bernardini IM, Kuo Y-M, Gahl WA, Nussbaum RL J Am Soc Nephrol. 2011 22: 443-8

Lowe Syndrome protein OCRL1 supports maturation of polarized epithelial cells. Grieve AG, Daniels RD, Sanchez-Heras E, Hayes MJ, Moss SE, Matter K, Lowe M, Levine TP. PLoS One. 2011 6:e24044

A small molecule mimicking a phosphatidylinositol (4,5)-biphosphate binding pleckstrin homology domain. Mak LH, Georgiades SN, Rosivatz E, Whyte GF, Mirabelli M, et al. ACS Chem Biol. 2011 6:1382-90

The Lowe syndrome protein OCRL1 is involved in primary cilia assembly. Coon BG, Hernandez V, Madhivanan K, Mukherjee D, Hanna CB, et al. Hum Mol Genet. 2012 21:1835-47

Inositol 5-phosphatases: insights from the Lowe syndrome protein OCRL. Pirruccello M, De Camilli P. Trends Biochem Sci. 2012 37:134-43

Lowe syndrome: Between primary cilia assembly and Rac1-mediated membrane remodeling. Madhivanan K, Mukherjee D, Aguilar RC. Commun Integr Biol. 2012 5:641-4

Impaired neural development in a zebrafish model for Lowe syndrome. Ramirez IBR, Pietka G, Jones DR, Divecha N, Alia A, Baraban SC, Hurlstone AFL, Lowe M. Hum Mol Genet 2012 21:1744-59

The Cellular and Physiological Functions of the Lowe Syndrome Protein OCRL1. Mehta ZB1, Pietka G, Lowe M. Traffic. 2014 Feb 5. doi: 10.1111/tra.12160

Mistargeting of peroxisomal EHHADH and inherited renal Fanconi's syndrome. Klootwijk ED, Reichold M, Helip-Wooley A, Tolaymat A, Broecker C et al. N Engl J Med. 2014 370:129-38

The Lowe Syndrome Protein OCRL1 Is Required for Endocytosis in the Zebrafish Pronephric Tubule. Oltabellla F, Pietka G, Ramirez IB, Mironov A, Starborg T, et al. PLoS One. 2015 11:e005058

Ciliopathies: The Trafficking Connection. Madhivanan K, Aguilar RC. Traffic 2014 15:1031-56

Role of Ocr1 in Primary Cilia Assembly. Madhivanan K, Ramadesikan S, Aguilar RC. Int Rev Cell Mol Biol. 2015 317: 331-347

Role of Ocr1 and Inpp5E in Primary Cilia Assembly and Maintenance. Madhivanan K, Ramadesikan S, Aguilar RC. Res Rep Biol 2016 7:15-29

Autophagosome-lysosome fusion triggers a lysosomal response mediated by TLR9 and controlled by OCRL. De Leo MG, Staiano L, Vicinanza M, Luciani A, Carissimo A, et al. Nat Cell Biol 2016 18:839-50

OCRL1 engages with the F-BAR protein pacsin 2 to promote biogenesis of membrane-trafficking intermediates. Billcliff PG, Noakes CJ, Mehta ZB, Yan G, Mak L, et al. Mol Biol Cell 2016 27:90-107

Kidney Tubular Ablation of Ocr1/Inpp5b Phenocopies Lowe Syndrome Tubulopathy. Inoue K, Balkin DM, Liu L, Nandez R, Wu Y et al. J Am Soc Nephrol 2017 28:1399-407



International Symposia

International Scientific Research Symposia

The *LST* also support and organise a number of international Lowe Syndrome research symposia where medical and scientific researchers present their latest findings, share ideas and form collaborations.

The first international medical conference on Lowe Syndrome was held at the National Institutes of Health (NIH) in Bethesda, Maryland USA in October 2002. The event was supported by a grant from the USA Office of Rare Diseases, the *Lowe Syndrome Association USA* (LSA) and the *Lowe Syndrome Trust*. The meeting was attended by about 30 people,



with some parents and a specially invited group of distinguished doctors and researchers from across the USA, England, France and Italy from disciplines including ophthalmology, neurology, nephrology, dermatology, dentistry and endocrinology. The purpose of the meeting was to discuss the clinical problems in Lowe Syndrome, consider issues relating to treatment and identify possible avenues for clinical research.



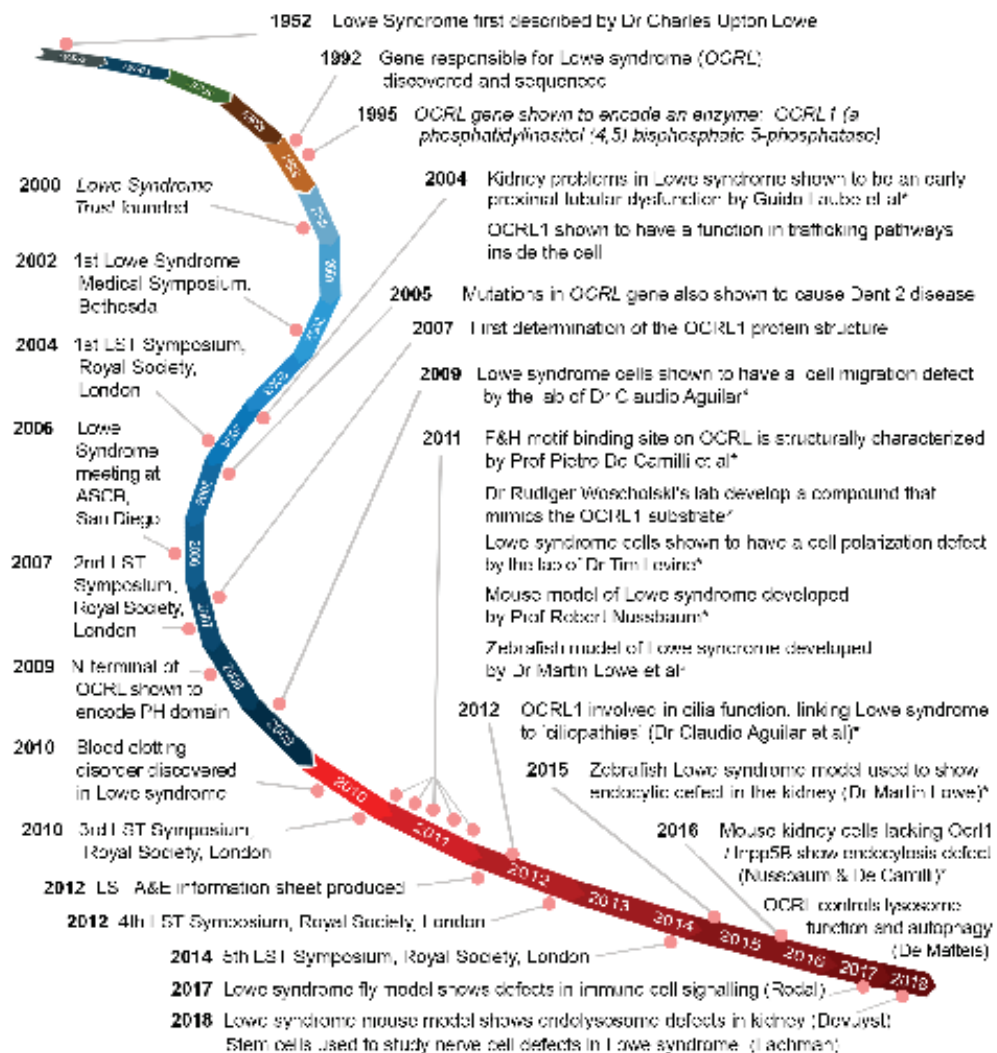
The second symposium was held by the *LST* at the Royal Society, Pall Mall, London in 2004, followed by a meeting in 2006 at the American Society of Cell Biology (ASCB) meeting in San Diego.



The *LST* has organised four further symposiums in London in 2007, 2010, 2012 and most recently at the Royal Society in London in December 2014, which included talks on cutting-edge stem cell research from eminent guest speakers Bruce Conklin (UCSF) and Juan Carlos Izpisua Belmonte (Salk Institute).

How far we have come...

Searching for a cure for Lowe syndrome will take time, but there have been many major advances in research, and the speed of discovery is increasing. So it's good to look back and see how far we have come and think about how soon more donations will bring about the next breakthrough.



* denotes projects funded by grants from the Lowe Syndrome Trust