



Since the last Newsletter at the beginning of 2008, the charity has funded four research grants totaling an amount of over £300,000. Dr Martin Lowe, Manchester University, Dr Claudio Aguilar at Purdue University in the USA and two grants to Professor Robert Nussbaum at the Institute of California in the USA. The Trust has also announced a new £80,000 Call for Research March 09. The Trust continually works on campaigns such as enticing schools to raise funds, payroll giving through company paye, Wills to charity, trust funding and writing to companies to entice donations. The Trust also writes grant applications to organisations such as The Lottery. We are still actively marketing the Lowe Syndrome bracelet and necklaces when the charity benefits by £10 for every item sold.

Events and Campaigns

May 08

The Lowe Syndrome Trust Mayfair Ball with Bryan Ferry

The Mayfair Ball organised by Threes A Crowd was an outstanding success. The evening commenced with a champagne reception followed by Three course dinner with a bespoke menu created by One Hundred One, unique to the event. Chef's who contributed to each course were Marcus Wareing, Atul Kochar and Michael Caines.



Entertainment for the evening started with Dynamo, one of the most important creative forces in magic today. Following an emotional recording of two mothers talking about how Lowe syndrome has affected their children... Scala, the all girl electric string quartet whom appeared on Britain's Got Talent, brought the audience alive with their rendition of Karl Jenkins's Palladio. Lowe Patron, Christopher Biggins took to the stage as guest Auctioneer and raised a staggering £42,000 for the charity with items such as dinner with Rod and Penny Stewart. The star performer of the evening was Bryan Ferry who sang old favourites such as Slave to Love, Jealous Guy and Let's Stick Together.

June 08

The Lowe Syndrome Trust Charity Bike Challenge Tuscany

A team of Lowe supporters organised by Lowe Patron, Mick Fennings took part in a four day charity cycle ride across the hills of Tuscany raising almost £30,000 – thank youboys!



September 08
The Lowe Syndrome Trust Charity Wine Tasting Evening

The Lowe Syndrome Trust
Charity Wine Tasting evening
Sponsored by Schroders
6.30pm, Thursday 11 September 2008

Join us for a fun wine tasting quiz evening which will raise funds to support medical research into Lowe Syndrome, a rare incurable children's disease.

The Lowe Syndrome Trust is a small UK charity.
 Visit www.lowetrust.com

RSVP Lorraine
0208 458 6791 / 07958 444020
lowetrust@homechoice.co.uk

Venue
SCHRODERS
31 Gresham Street
London EC2V 7QAV

Ticket
 £45
 No

And Noah he often said to his wife when he sat down to dine, I don't care where the water goes if it doesn't get into the wine.
 G.K. Chesterton (1874-1936)
 Wine and Water

Our thanks to Alan Brown of Schroders who kindly organised a wine tasting evening to raise funds to support research into Lowe Syndrome. The evening was a fabulous success tasting fine wines organised by Alan who also gave a short presentation on the wines that evening. The evening raised just over £5,000 for Lowe medical research.

December 08
The Lowe Syndrome Trust Christmas Charity Evening

The Lowe Syndrome Trust
Charity Event
7:30pm Sunday 30th November 2008

THE AM BAND PRESENTS
"A CHRISTMASSOUL"

Join us for a fun evening at *La Pigalle* for the premier of the Lowe Syndrome Trust charity christmas album. The AM Band have kindly recorded and produced the album "A Christmassoul" with all proceeds to the charity.

The evening will also include a performance by

The **Big Funk Corporation** and the fabulous **Fabbagirls**

The Lowe Syndrome Trust is a small UK charity raising funds to support medical research into Lowe Syndrome, an incurable children's disease.
 Visit www.lowetrust.com

RSVP Lorraine
0208 458 6791 / 07958 444020
lowetrust@homechoice.co.uk

Ticket
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Andy Mitchell of the Big Funk Corporation kindly produced a Lowe Christmas charity album which was premiered at La Pigalle Sunday 30th November. Andy and the AM Band performed songs from the album and Lowe Patrons The Fabbagirls performed a host of Abba songs. Our thanks to the owner of La Pigalle, Vince Power, who supported the Trust that evening.

Details of the Christmas album are attached. The Trust is at present marketing the album to shops for Christmas 2009. If you have any contacts please let us know!

December 08
Medical Innovations Awards 2008

The Lowe Syndrome charity was invited to the 2008 Medical Futures Innovations Awards dinner on 3rd December 2008. The event, held at the Honourable Artillery Company Ground in London, was hosted by Melanie Sykes and comedian David Mitchell, with a distinguished audience of 800 top business leaders, medical and scientific experts, and policy makers.



The Awards take ideas from frontline healthcare professionals, managers and academics, and help catalyse them to success. Working hand-in-hand with the medical and scientific key representative bodies, the awards encourage, support and reward clinical and commercial excellence. Awards were won for a series of novel products and services including a form of injectable bone, a stem cell therapy to repair damaged cardiac muscle, a dental imaging technique that does not use x-rays, targeted genetic techniques to optimise cancer treatments and a portable hand held hearing device to detect hearing loss in less than 30 seconds.

The board and Patrons of the Lowe Syndrome Trust charity (pictured) were invited as guests to this private function. Trustee's Lorraine Thomas and Jonathan Ross presented the work of the charity and also auctioned Jonathan's motor scooter, tickets to the BAFTA awards and also a picture donated by Penny and Rod Stewart, who are also patron's of the Lowe charity.



May 2009
CYCLE CHALLENGE WINE EVENING EPPING

Penny Lancaster Stewart and Rod Stewart took time out of their busy diary to attend a very small charity event at the SpeakEasy Bar in Epping near the couple's home. The evening was to raise funds for vital medical research into Lowe Syndrome, an incurable children's disease. Penny has been a Patron of the charity for the past five years helping raise the profile of the charity, awareness of the disease and funding to support research.

Penny commented "Each year I do my bit but that's just the tip of the iceberg – the charity needs to treble its funds to enable a cure to be found. The Trust is organising a 10th year anniversary ball next year and so any companies out there wishing to sponsor the evening should get in touch with Lorraine Thomas, founder of the charity (details below).

The evening was a great success with entertainment by Martin Bellamy whom is best known as one half of the duo Bell and Spurling who had two top 10 hits with their famously self penned songs "Sven sven Sven" and "Goldenballs" selling over 300,000 singles and appearing on numerous albums selling all over Europe. Martin has appeared on virtually every major TV entertainment show including two live appearances on Top of the Pops.

An auction included items such as VIP tickets for both the Michael Jackson and Spandau Ballet concerts to be held later this year, a pair of shoes signed and donated by Dame Shirley Bassey and an Arsenal Football shirt signed by the team. Owner of the Speakeasy Bar, Martin Bell, said he was delighted to support such a worthy cause.



June 2009

Low Syndrome Trust Cycle Challenge Sicily



The annual cycle ride organised by Mick Fenning was a wonderful success with the exception of a serious accident – Danny Farmer completed the challenge but on the home stretch to the hotel had to break suddenly at a speed of 40mph falling off his bike luckily missing a wall. He sustained a broken arm and leg requiring 4 hour surgery to insert metal plates. He is recovering well and more concerned about Oscar who has Lowe syndrome who visited him whilst in Sicily!

The event raised almost £25,000 – a fantastic achievement in spite of the present economic climate.

March 09

Dents/Lowe Symposium The Royal Free Hospital, London

Low Syndrome and Dents – a new discovery.

The Low Syndrome Trust sponsored a kidney meeting at the Royal Free Hospital March 09. We were delighted to support the attendance of Steven J Scheinman from the USA who discussed the findings that 15% of patients with Dent's disease have mutations in OCRL1, the gene responsible for Lowe Syndrome.

The symposium was organised to honour Professor Oliver Wrong on the occasion of the 50th anniversary of the publication of his classic paper on measuring how the kidney excretes acid from the body. Prof. Wrong worked closely with Professor Charles Dent, who from the 1950s until his death in 1976 made many pioneering discoveries regarding mineral metabolism and kidney function. Prof. Dent described several patients in studies subsequently augmented by Prof. Wrong, leading to the discovery of what we now call "Dent's disease". The kidney problems include loss of proteins, minerals, and other solutes in the urine, and eventual renal failure. These features resemble identically the kidney problems seen in patients with the Lowe syndrome, but patients with Dent's disease do not have the renal acidosis, mental developmental delay, or eye problems that are so characteristic of LS. It is well established that Dent's disease is associated with

mutations in a gene, *CLCN5*. However, we found that about 40% of patients with Dent's disease do not have mutations in this gene, and surprisingly that about 15% of these have mutations in *OCRL1*, the gene responsible for LS. This observation has now been confirmed by laboratories in Germany and Japan as well as ours.

It is remarkable that even those patients with Dent's disease whose mutation is in *OCRL1* lack the severe eye, brain, and acidosis problems that LS patients have. A possible explanation for this mystery is now emerging. We and others have observed that the pattern of mutations in *OCRL1* in these patients differs from that in LS patients. These differences suggest that there are different forms of the *OCRL1* gene in different tissues of the body, so that mutations in one part of the gene would alter its function in the kidney but perhaps not in the eye or brain, or the cells involved in urinary acid excretion. These observations need to be pursued in further studies, but offer the hope of understanding better the mechanisms that produce the most disabling features of the

LOWE SYNDROME TRUST PRESS RELEASE – MARCH 2008 **THREE RESEARCH PROJECTS FUNDED BY THE UK LOWE SYNDROME TRUST**

Innovative new study of Lowe syndrome underway. Scientists are to take three different approaches to find a cure for rare genetic condition Lowe syndrome.

The inherited condition, found only in boys, can produce cataracts of the eyes, defects in brain development and kidney problems. Life expectancy is short due to the complications associated with the disease, which include blindness, arthritis, rickets, mental impairment and development delay. Three grants, totalling £240,000, have been given by the Lowe Syndrome Trust to fund three unique projects researching the illness.

One common link between all three is in the study of the gene *OCRL1*, a key factor in the cause of the disorder. At the University of Manchester, a pilot study previously found that the gene works in a similar manner in zebra-fish as it does in humans, and therefore, will be using the fish to aid study. Dr Martin Lowe, leading this innovative research, said:

"Zebra-fish offer a number of advantages over other model systems and we plan to extend our earlier analysis to further scrutinise the role of *OCRL1* in development, focusing initially on the brain but also examining the other tissues affected in Lowe syndrome.

"In the long term, it is hoped that zebra-fish will serve as a model system for experimenting with chemicals that suppress the symptoms of Lowe syndrome in the hope of one day finding a cure."

At Purdue University in Indiana, USA, a team led by Dr Claudio Aguilar, will study the cellular consequences of Lowe syndrome. Dr Aguilar said:

*"Our laboratory recently found that cells from Lowe syndrome patients are deficient for crawling and spreading on biological surfaces. Since these processes play a crucial role during embryo development, we believe that this faulty behaviour may contribute to the onset of the disease. Thanks to the support provided by the Lowe Syndrome Trust, we are going to be able to investigate the causes of these abnormalities...Biochemical experiments conducted by our team further indicate that *OCRL1* interacts with the cellular machinery that dictates how cells relate to their environment. Thus, our research will also be directed towards gaining insight about how patient cells sense their surroundings and absorb nutrients. We will assess the functionality of intake routes in patient cells as these paths are key to the success of therapeutic countermeasures...This research, made possible by generous support provided by the Lowe Syndrome Trust, will help us to gather precious information about the cellular manifestations of this illness. Ultimately, we hope that a better understanding of the underlying mechanism will help to design new therapeutic approaches to fight this debilitating disease".*

The third grant awarded by the Lowe Syndrome Trust will be used to help continue work already underway at Imperial College, London. Drs Woscholski and Vilar have been developing chemical tools for the detection of the substrates of the *OCRL1* enzyme since 2003. This work has generated chemical compounds that are able to recognise the *OCRL1* substrate with some selectivity in conditions that mimic the cellular environment.

Drs Woscholski and Vilar have continued to work on the characterisation of these new compounds in living cells, and are able to study the suitability of the receptors towards generating chemical tools for biomedical research and which may even provide the foundations of a future drug development programme to tackle the symptoms of Lowe Syndrome.

Lowe syndrome was first recognised in 1952 by Dr Charles Lowe and is caused by a gene mutation which makes a defective version of an enzyme named OCRL1, needed for normal function of tissues like the lens, brain and kidney, although the reasons for this mutation are still quite unclear.

The Lowe Syndrome Trust (LST) was set up by Lorraine Thomas as a voluntary charity in June 2000 when her son, Oscar (then aged 5), was diagnosed with the disease. The Trust supports researchers worldwide in their efforts to gain knowledge and tools to tackle this devastating disease.

For further information, contact Lorraine Thomas at the Trust on 020 8458 6791/020 7794 8858/07958 444020; email LST@lowetrust.com or visit the website at www.lowetrust.com.