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 zebrafish as it does in humans, and therefore, will be using the fish to aid study. Dr Martin Lowe, leading this innovative research, said:

"Zebrafish 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 zebrafish 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."

And 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 mperial 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 lowetrust@homechoice.co.uk or visit the website at www.lowetrust.com