The Lowe Syndrome Trust announces new Medical Research Grant to Professor Robert Nussbaum, MD, Institute of California, USA

The Lowe Syndrome Trust announces the extension of its grant to Dr. Robert Nussbaum at the University of California School of Medicine for a third year of support of his proposal "Creating a mouse model of Lowe Syndrome". This support will allow Dr. Nussbaum to characterize a novel strain of mice he has developed, with the support of the Lowe Syndrome Trust, that mimics the genetic changes seen in patients with Lowe Syndrome. In his Progress Report to the Trust, Dr. Nussbaum reports that the new strain of mice, which were designed to recapitulate the biochemical and metabolic alterations seen in patients with Lowe syndrome, recapitulates, for the first time, the changes in kidney function seen in this condition. The availability of the mouse model will allow a much more detailed characterization of how a defect in the Ocrl1 phosphatidylinositol 4,5 bisphosphate 5-phosphatase enzyme leads to the disease and, more importantly, will provide a critical model system for developing and testing new therapies for preventing or reversing me of the Syndrome's most serious abnormalities

Dr. Nussbaum's laboratory studies genetic contributions developmental and neurodegenerative disorders. His two major areas of concentration are Lowe syndrome and Parkinson disease. Lowe syndrome, formally known as Lowe oculocerebrorenal syndrome (OCRL), is a rare X-chromosome-linked disorder that can cause mental retardation, seizures, cataracts, and kidney disease in young children. Most Lowe syndrome patients die in their teens or twenties. Parkinson disease is a slowly progressive disease of the nervous system, which strikes an estimated 50,000 mostly older Americans each year. It is second only to Alzheimer's disease among the most common neurodegenerative diseases in the developed world.

In 1992, Dr. Nussbaum identified a defective gene that causes Lowe syndrome. The gene, *OCRL1*, codes for phosphatidylinositol-4, 5-bisphosphate 5-phosphatase-an enzyme that acts primarily in the Golgi apparatus of the cell and may be involved in protein processing and transport. Dr. Nussbaum's lab developed a clinically useful enzyme test for Lowe Syndrome, carried out the first prenatal diagnosis of the condition by enzyme assay, and pioneered the delivery of genetic services and counseling, including carrier testing, to families of Lowe syndrome patients. Determining the enzyme's normal function and why disabling it affects so many apparently unrelated organ systems could point to possible treatments. Interestingly, *OCRL1* knockout mice do not develop Lowe syndrome symptoms. Dr. Nussbaum is investigating the role of an autosomal paralog for *OCRL1, INPP5B*, as a possible compensating gene and gene product in mice