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Unlocking the mystery of Lowe

Reporter finds out about Imperial's innovative research into the genetic condition Lowe syndrome

Dr Rudiger Woscholski (Cell and Molecular Biology) and Dr Ramon Vilar (Chemistry) have been conducting research on Lowe syndrome since 2003 when they received £50,000 of funding from the Lowe Syndrome Trust for a three-year chemistry PhD geared towards developing a reliable tool for diagnosing the syndrome.

Lowe syndrome is a rare genetic condition found only in boys, which can produce cataracts in the eyes, defects in brain development and kidney problems and as a result can lead to short life expectancy.

The syndrome was first recognised in 1952 by Charles Lowe and is caused by a gene mutation which makes a defective version of an enzyme named OCRL1. This enzyme removes phosphates from a signalling lipid called PIP2, which seems to be responsible for normal function of tissues, particularly in the lens, brain and kidney.

Having a defective OCRL1 enzyme (which is known as a phosphatase) means that carriers experience elevated levels of PIP2, which is known to interact with proteins determining cell shape as well as intracellular transport and uptake mechanisms. It is not clear how the elevated PIP2 levels can bring about the symptoms observed in Lowe syndrome and neither is there a formal treatment route available.

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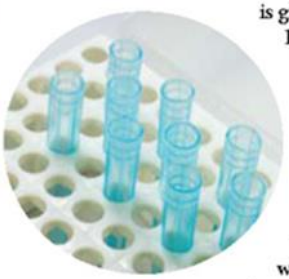
Raising awareness

The Lowe Syndrome Trust was set up eight years ago by Lorraine Thomas when her son Oscar was first diagnosed with the disease. She explains: "At the time I met with various government officials who confirmed there was no UK research and no official statistics. It has been an uphill struggle raising awareness but today the Trust is the main charity in the world funding research into the disease and we have lots of supportive patrons, including former Rector Sir Richard Sykes."

Dr Woscholski explains what sparked his interest in the syndrome: "As a scientist my specialism is lipid phosphatases – so having the opportunity to study the role of PIP2 in more detail is incredibly interesting. And speaking as a parent, I think the project is incredibly worthwhile – there are so many unknowns for our children and I am lucky to be in a position to try and help by looking at one of them."

Developing a diagnostic tool



Dr Woscholski and Dr Vilar worked to develop a chemical, which could form the template for future diagnostic tools or ultimately drugs. It was envisaged that the former could be used to develop a method for the detection of elevated PIP2 levels in patients.

In 2006 when the funding for the PhD had come to an end and a couple of promising chemicals were produced, the Lowe Syndrome Trust gave Imperial a six-month extension for the project so they could take it a step further and test their biological potential. In addition, the Chemical Biology Centre at the College awarded an £87,000 grant to the research team to continue their work on the chemistry side.

The new funding allowed Evelyn Rosivatz, a pharmacologist in the Division of Cell and Molecular Biology, to be brought onto the project to test the chemicals on cells. The idea was to see if the chemicals Dr Woscholski and Dr Vilar had developed would behave in the same way as they did during the chemical tests.

Dr Woscholski describes what happened over the next six months: "Evelyn discovered that the chemical we had developed does bind PIP2 in the cells and thus reduce their levels. These encouraging results imply that the first steps towards a cure have been taken."

Next stage

This term the Lowe Syndrome Trust has provided a third grant for Evelyn to conduct a biology PhD over the next three years. Dr Woscholski says: "Evelyn will look at how PIP2 is affecting cellular behaviour employing the chemicals obtained in live cells. The aim is to explain the PIP2 dependent pathways that are governing the development of Lowe syndrome."

The work the scientists are doing is giving hope to families who have children with Lowe syndrome. As Lorraine Thomas explains: "We are excited about the work at Imperial as it may produce a drug to emulate the missing enzyme. I am not sure whether any of our projects will ever help our son Oscar because of the length of time each project will take but I live in hope, and if I can double the amount raised then we can fund more vital research."

— Emily Ross, Communications

Applications for a new £80,000 Lowe Studentship grant are open until 30 September. For more details please contact Lorraine Thomas: **lowetrust@homechoice.co.uk**