LOWE SYNDROME RESEARCH MEETING 2023

SCIENCE PRESENTATION SUMMARIES

LSA LOWE SYNDROME ASSOCIATION

LST The Lowe Syndrome Trust
Care Today… Cure Tomorrow

AiSLo

Gurdon INSTITUTE

Gene
OCRL1

OCRL1

Dent 2 disease

Lowe syndrome

Gene
OCRL1

OCRL1

KIDNEY

BRAIN

EYE

GROWTH

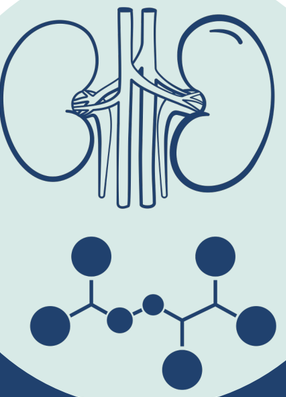
BLOOD

CLAUDIO AGUILAR

His research team is looking at different genetic mutations in Lowe syndrome patients. They found that not all mutations have the same effects on the OCRL1 protein. In future this could help us understand the different symptoms in Lowe syndrome patients.

What symptom are you trying to impact?

As many as possible: we are trying to understand how the gene mutations cause the symptoms.



What are your goals short term and long term?

In the short term, find the link between the gene mutation and function of the OCRL protein.

Long term to create new therapies.

ANTONIJA JURAK BEGONJA

Some Lowe Syndrome patients have bleeding problems during surgery. Her team found that functional OCRL protein is needed for normal blood clotting. They are studying how this is related to the genetic changes in Lowe syndrome.

What symptom are you trying to impact?

The reported bleeding disorder associated with Lowe syndrome.

What are your goals short term and long term?

Short term to describe how particular cells in the blood called platelets are affected.

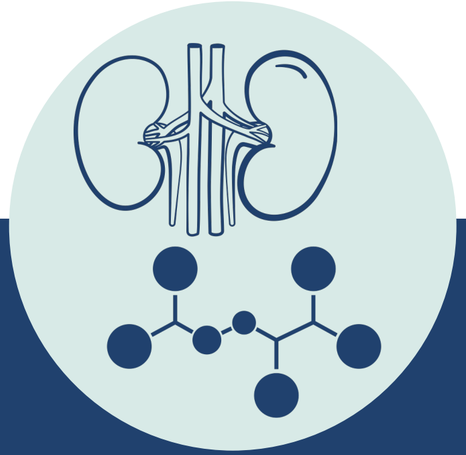
Long term, a better understanding of the molecular basis of platelet function.

ANTONELLA DE MATTEIS

Her team are finding new treatments by testing different drugs and using advanced imaging techniques. The most effective drugs for improving the cell changes are then tested in mice with a condition similar to Lowe syndrome.

What symptom are you trying to impact?

As many as possible, particularly the loss of chemicals and proteins in the urine by the kidney.



What are your goals short term and long term?

To give new treatments for people with Lowe syndrome.

ARNAUD ECHARD

His research team found that cells use certain proteins to control the way cells move substances around inside them. This knowledge can help us understand how Lowe syndrome affects cells.

What symptom are you trying to impact?

As many as possible, I am trying to understand what happens inside cells.

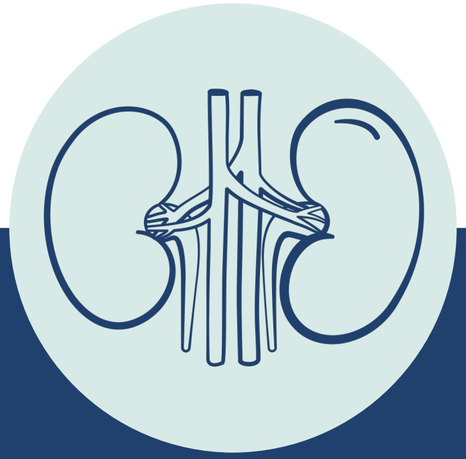
What are your goals short term and long term?

Short term to have a detailed understanding of how cells move substances around inside them.

Long term to see how this helps others working on the symptoms of the disease.

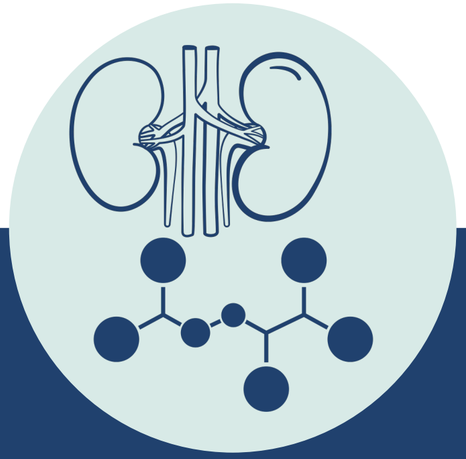
FRANCESCO EMMA

Kidney problems in Lowe syndrome are called Fanconi syndrome. Francesco is an expert in how to measure and monitor this condition and is looking at how to use this information in clinical trials.



What symptom are you trying to impact?

The kidney imbalance and loss of valuable chemicals and proteins in the urine.

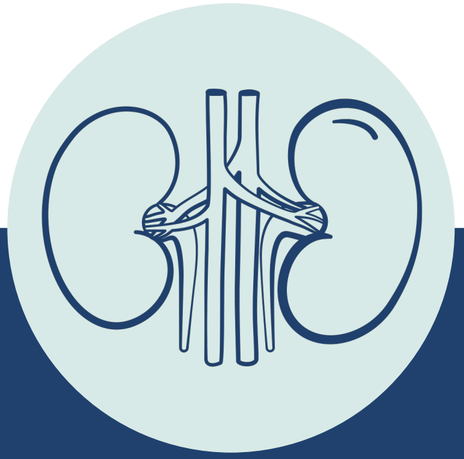


What are your goals short term and long term?

To establish a clinical trial protocol that will lead to approved drugs for these types of kidney diseases.

KAI ERDMANN

His research team is developing and using tiny organ models to study Lowe syndrome. They found that these models can mimic the disease and help test new treatments.



What symptom are you trying to impact?

The loss of chemicals and proteins in the urine by the kidney.

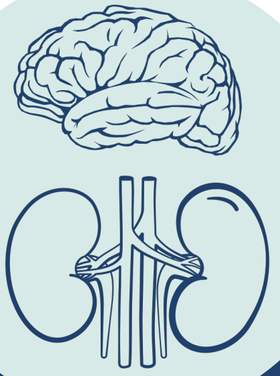
What are your goals short term and long term?

To establish human tissue models of Lowe syndrome so it can be studied in more accurate ways.

In the longer term to understand more about the symptoms seen in Lowe syndrome and to discover drugs that can help.

JENNY GALLOP

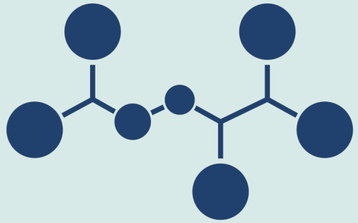
Her research team are finding out how changes in fatty chemicals in Lowe syndrome affect cells. They tested a medicine that might improve kidney function in Lowe syndrome patients. They are now studying how this medicine affects brain cells.



What symptom are you trying to impact?

The kidney and starting to look at the brain.

We are trying to understand how the microscopic chemistry of the cells is altered and how to fix it.



What are your goals short term and long term?

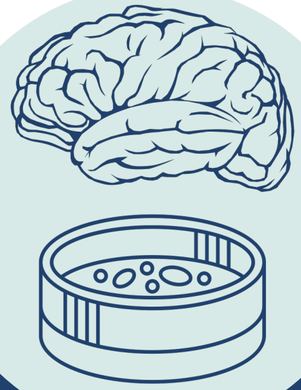
To see if a new medicine (alpelisib) will be of help. In short term in the kidney and longer term in the brain.

HERB LACHMAN

His research team has made a model using stem cells to study the brain and mental aspects of Lowe syndrome. They used cells from patients with certain gene mutations. They found that some mutations were worse than having no gene at all. This can help find new ways to treat Lowe syndrome.

What symptom are you trying to impact?

Learning disabilities and neuropsychiatric symptoms.



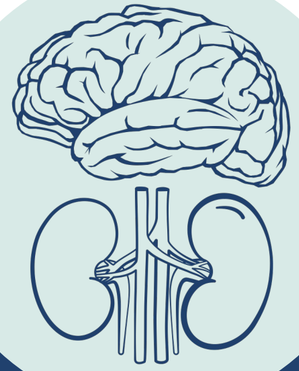
What are your goals short term and long term?

Short term to understand how patient mutations affect brain cells.

Long term to understand what is going wrong in the brain and how to fix it.

MARTIN LOWE

His research team are using genetically altered fish to study Lowe syndrome. They found problems in the fish nervous system and kidneys. These fish models can help us understand and treat Lowe syndrome.



What symptom are you trying to impact?

How the brain forms during development and the kidney symptoms.

What are your goals short term and long term?

To model the disease most effectively in a cheap and easy animal model: the zebrafish.

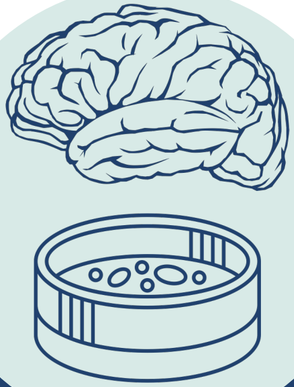
To understand how tissues are changed in Lowe syndrome so we can work out ways to help.

RAGHU PADINJAT

His team are using stem cells from Lowe syndrome patients to study brain development. They found changes in brain cell differentiation and function.

What symptom are you trying to impact?

The brain, specifically developmental delay.



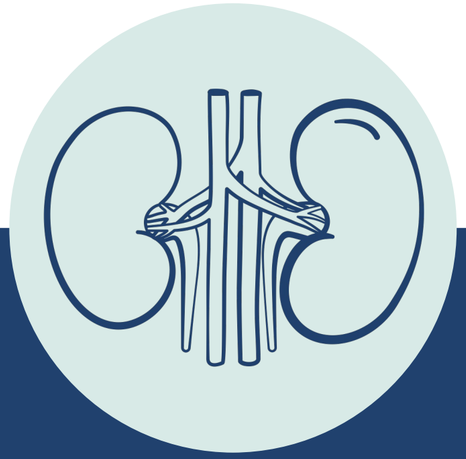
What are your goals short term and long term?

Short term to develop brain cell models to understand the disease.

Long term to understand how the brain develops differently.

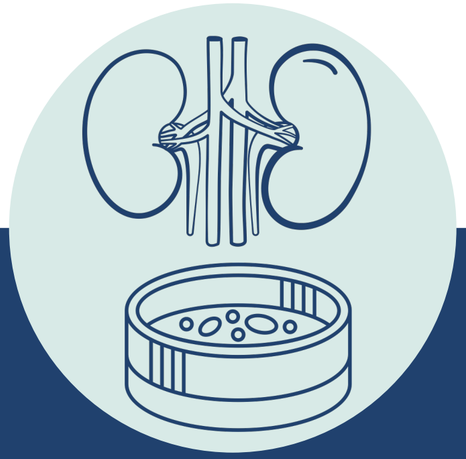
LEOPOLDO STAIANO

He and his team are studying how the OCRL1 gene and altered fatty chemicals in cells affect kidney function in Lowe syndrome. They found that this can lead to kidney damage. They are using tiny organ kidney models to study the disease and find new treatments.



What symptom are you trying to impact?

Kidney symptoms, increased protein in the urine and chronic kidney disease.



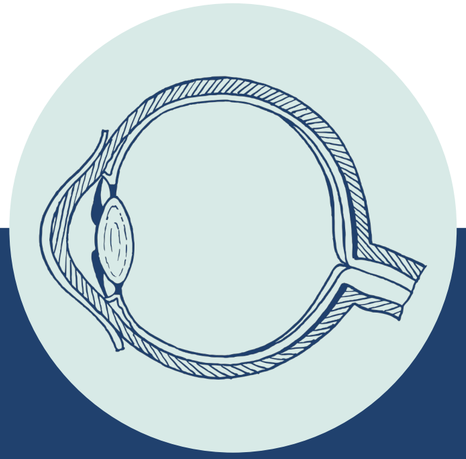
What are your goals short term and long term?

Short term to understand the cellular changes in the kidney.

Long term understand how the mutations are leading to kidney failure.

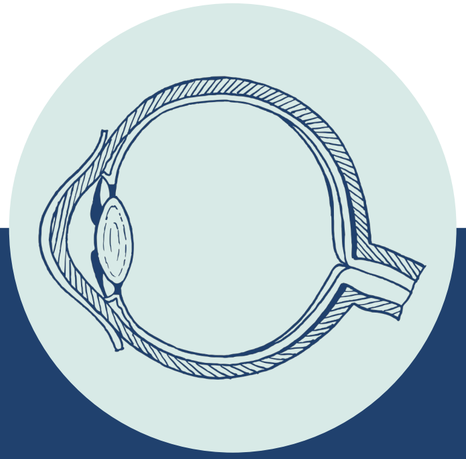
YANG SUN

Children with Lowe syndrome often have eye problems, like cataracts and vision loss. His research team is studying these eye problems to better understand and treat them.



What symptom are you trying to impact?

The different types of eye conditions, including cataracts, glaucoma, scarring and lazy eye.



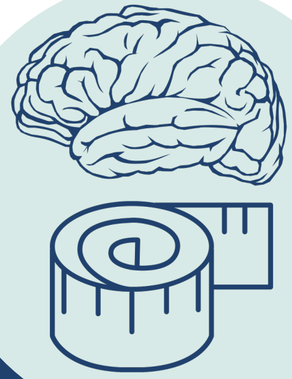
What are your goals short term and long term?

Short term to have a better understanding of the eye diseases in Lowe syndrome.

In the long term to help LS patients see better.

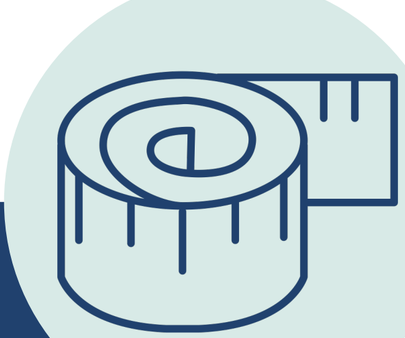
VIDHU THAKER

Her research team are studying how small differences in the OCRL1 gene affects the brain. This may help us understand how Lowe syndrome affects growth.



What symptom are you trying to impact?

Short stature and control of body functions.



What are your goals short term and long term?

To establish how the brain and hormone systems are affected.

In the longer term to establish evidence for or against human growth hormone as a therapy.

GLOSSARY OF TERMS

- Alpelisib: A drug used to treat certain types of breast cancer, and has potential therapeutic effects on Lowe Syndrome.
- Chronic kidney disease (CKD): A condition in which kidney function gradually declines over time, potentially leading to kidney failure.
- Congenital cataracts: Clouding of the eye lens present at birth, which can cause vision problems.
- CRISPR-Cas9: A tool used to edit genes by adding, removing, or changing specific DNA sequences.
- Cytokinesis: The process by which a cell divides into two daughter cells during cell division.
- Cytoskeleton: A network of proteins within a cell that provides structural support and plays a role in various cellular processes.
- Endocytosis: The process by which cells take in molecules from the environment by engulfing them in their membrane.
- Epithelial-mesenchymal transition (EMT): A process by which epithelial cells, which line organs and blood vessels, transform into more mobile and invasive mesenchymal cells. This process is involved in tissue repair, but can also contribute to disease progression.
- F-actin: A protein that forms the structure of cells and is involved in various cellular processes.
- Fanconi syndrome: A kidney disorder causing excessive loss of nutrients and electrolytes in the urine.
- Hemostasis: The process by which blood flow is stopped after an injury.
- Induced pluripotent stem cells (iPSC): Adult cells that are reprogrammed into a state similar to embryonic stem cells, capable of developing into different cell types.
- Lipid droplets (LDs): Storage compartments within cells that hold lipids, or fat molecules.
- Lowe Syndrome (LS): A rare genetic disorder affecting the eyes, brain, and kidneys, causing congenital cataracts, intellectual disabilities, and kidney problems.
- Neuroendocrine pathways: Communication networks between the nervous system and the endocrine system, responsible for regulating hormone release.
- Neural progenitor cells (NPCs): A type of precursor cell that can give rise to different types of cells in the nervous system.
- Nuclear medicine scans: Imaging tests that use small amounts of radioactive materials to diagnose and treat various diseases.
- OCRL1 gene: A gene responsible for encoding the enzyme OCRL1, mutations in which can lead to Lowe Syndrome.
- Organ on a chip: A microfluidic device that simulates the functions of an organ, providing a more realistic environment for studying diseases and testing drugs.
- Organoid: A three-dimensional, miniaturized, and simplified version of an organ, grown in vitro from stem cells. Organoids mimic the structure and function of their corresponding organ, providing a valuable tool for studying organ development, disease modeling, and testing potential treatments.
- Peroxisomes: Small cellular structures involved in the breakdown of fatty acids and the elimination of toxic substances.
- Phosphatidylinositol (4,5) bisphosphate (PI(4,5)P2): A type of lipid molecule found in cell membranes that plays a crucial role in cell signaling and membrane trafficking.
- Platelets: Blood cells that help form clots to stop bleeding.
- WAVE1: A protein involved in the regulation of actin polymerization, which is essential for cell shape and movement.
- Zebrafish: A small tropical fish used as a model organism for studying human diseases.