OCRL gene

OCRL, inositol polyphosphate-5-phosphatase

Normal Function

The *OCRL* gene provides instructions for making an enzyme that is present in cells throughout the body. This enzyme is part of a larger group of enzymes that modify fat (lipid) molecules known as membrane phospholipids. These molecules form the basic structure of cell membranes. Specifically, the OCRL enzyme regulates the levels of a membrane phospholipid called phosphatidylinositol 4,5-bisphosphate.

The OCRL enzyme is found in several areas within cells. It is concentrated in a complex network of membranes known as the trans-Golgi network, which sorts proteins and other molecules and sends them to their intended destinations inside or outside the cell. The OCRL enzyme is also found on endosomes, specialized compartments that are formed at the cell surface to carry proteins and other molecules to their destinations within the cell.

By controlling the level of phosphatidylinositol 4,5-bisphosphate, the OCRL enzyme helps regulate the transport of certain substances to and from the cell membrane and chemical signaling between cells. The enzyme may also be involved in the regulation of the actin cytoskeleton, which is a network of fibers that make up the cell's structural framework. The actin cytoskeleton has several critical functions, including determining cell shape and allowing cells to move.

Recent research suggests that the OCRL enzyme is found in cell structures called primary cilia, which are microscopic, finger-like projections that stick out from the surface of cells and are involved in signaling pathways that transmit information between cells. Cilia are important for the structure and function of many types of cells, including cells in the brain, kidneys, and liver. Cilia are also necessary for the perception of sensory input (such as sight, hearing, and smell). Studies suggest that the OCRL enzyme may play a role in the formation, function, and maintenance of cilia.

Health Conditions Related to Genetic Changes

Dent disease

At least 20 mutations in the *OCRL* gene have been found to cause Dent disease 2. This form of Dent disease is characterized by chronic kidney problems; some affected individuals also have mild intellectual disability, weak muscle tone (hypotonia), and clouding of the lens of the eyes (cataract) that does not impair vision. Some researchers consider Dent disease 2 to be a mild variant of Lowe syndrome, which is discussed below.

The *OCRL* gene mutations that cause Dent disease 2 reduce or eliminate the function of the OCRL enzyme. These changes impair the transport of certain molecules and regulation of the actin cytoskeleton. They may also affect cell signaling by altering the structure or function of cilia. Disruption of these important cell activities likely impairs kidney function, leading to excess protein in the urine (proteinuria), kidney stones, and ultimately kidney failure. It is unknown how loss of the OCRL enzyme contributes to the other signs and symptoms of this condition.

Because the OCRL enzyme is present throughout the body, it is unclear why Dent disease 2 primarily affects the kidneys and, to a lesser extent, the brain, eyes, and other tissues. It is possible that other enzymes may be able to compensate for the defective OCRL enzyme in unaffected tissues.

Lowe syndrome

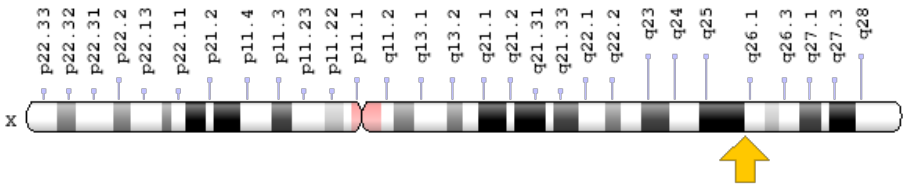
More than 120 mutations in the *OCRL* gene have been identified in individuals with Lowe syndrome, a condition that affects the eyes, brain, and kidneys. Some of these mutations prevent the production of any OCRL enzyme. Other mutations reduce or eliminate the activity of the enzyme or prevent it from interacting with other proteins within the cell. Researchers believe that the effects of these genetic changes are similar to those of the mutations that cause Dent disease 2: the mutations likely alter the transport of molecules within cells, regulation of the actin cytoskeleton, and the structure and function of cilia. It is unknown why some *OCRL* gene mutations cause Lowe syndrome and others cause Dent disease 2.

Because the OCRL enzyme is present throughout the body, it is unclear why Lowe syndrome primarily affects the kidney, brain, and eyes. As with Dent disease 2, it is possible that other enzymes may be able to compensate for the defective OCRL enzyme in unaffected tissues.

Chromosomal Location

Cytogenetic Location: Xq26.1, which is the long (q) arm of the X chromosome at position 26.1

Molecular Location: base pairs 129,540,259 to 129,592,556 on the X chromosome (Homo sapiens Updated Annotation Release 109.20190607, GRCh38.p13) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- INPP5F
- LOCR
- Lowe oculocerebrorenal syndrome protein
- NPHL2
- OCRL1
- OCRL_HUMAN
- oculocerebrorenal syndrome of Lowe
- phosphatidylinositol polyphosphate 5-phosphatase

Additional Information & Resources

Educational Resources

- Molecular Biology of the Cell (fourth Edition, 2002): Transport into the Cell from the Plasma Membrane: Endocytosis
  https://www.ncbi.nlm.nih.gov/books/NBK26870/
- The Cell: A Molecular Approach (second edition, 2000): The Golgi Apparatus
  https://www.ncbi.nlm.nih.gov/books/NBK9838/

Clinical Information from GeneReviews

- Dent Disease
  https://www.ncbi.nlm.nih.gov/books/NBK99494
- Lowe Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1480

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28OCRL%5BTIAB%5D%29+OR+%28OCRL1%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+2880+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- OCRL GENE
  http://omim.org/entry/300535

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_OCRL.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=OCRL%5Bgene%5D
- HGNC Gene Symbol Report
  https://www.genenames.org/data/gene-symbol-report/#!/hgnc_id/HGNC:8108
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:4952
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https://ghr.nlm.nih.gov/gene/OCRL

Reviewed: November 2013
Published: September 10, 2019

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