Novel therapeutic approach to Polycystic Kidney Disease

Technology #16389

Applications

This technology comprises a class of compounds, denoted 11β, and associated methods useful for the treatment of Polycystic Kidney Disease (PKD) by modulating the sensitivity to oxidative stress of the target cells.

Problem Addressed

PKD is among the most common life-threatening monogenic inherited diseases in the world. It is a leading cause of end-stage renal failure and a common indication for dialysis or renal transplantation. Currently, there are no FDA-approved therapeutic drugs available that directly target PKD. Clinical strategies (e.g., mTOR inhibitors) that have focused on slowing the growth of cystic cells have been largely ineffective. Through a different mechanism of action, in the cellular respiration pathway, the 11β molecules target affected cells with high specificity.

The inventors of this technology demonstrate that administration of 11β compounds to mouse models of PKD results in a significant reduction of kidney cyst formation, restoration of kidney size, and kidney function with no significant adverse toxic or metabolic effects. The inventors note that the activity of the compounds in a PKD animal model is substantially better than other reference compounds in the literature.

Technology

Inducing apoptosis by oxidative stress is a known mechanism for several compounds with clinical relevance. Cells lacking both copies of PKD genes (i.e., the cystic cells of PKD) are characterized by mitochondrial abnormalities that reduce their ability to respond to oxidative stress. In two distinct PKD1 conditional knockout mouse model, exposure to 11β increases oxidative stress in the cystic cells, leading to the destruction of the target cells via apoptosis while normal kidney cells remain unaffected. In these mouse models of PKD, treatment with 11β dramatically slows down the course of the disease and restores kidney size and function back to normal levels. The 11β class of molecules constitutes an effective small-molecule therapeutic for PKD, by selectively destroying the cyst-forming cells.

Advantages

- Selectively targets the cyst-forming cells in PKD
- Exposure to 11β molecules shows no significant adverse toxic or metabolic effects in unaffected organs
- Administration of 11β compounds to mice demonstrates the therapeutic benefits of the compounds such as regression in cyst size and number, and restoration of the kidney function *in vivo*

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- The mechanism of 11β molecules (i.e., targeted killing of cystic cells) suggests a possible intermittent clinical regimen (e.g., patients take the drug only a few weeks at a time, followed by recovery periods), which will greatly benefit patient compliance and quality of life. This is a huge advantage over a drug like Tolvaptan, which has to be administered continuously

Intellectual Property

IP Type: Granted US Patent

IP Title: Methods for treating polycystic kidney disease and polycystic liver disease

IP Number: 9,982,009

Categories For This Invention:

Life Sciences
Biotechnology
Clinical Applications
Therapeutics

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Publications:

Polycystin-1 a Master Regulator of Intersecting Cystic Pathways
Trends in Molecular Medicine
May 2014, Pages 251-260
Chemical Genetic Analysis of an Aniline Mustard Anticancer Agent Reveals Complex I of the Electron Transport Chain as a Target
The Journal of Biological Chemestry
September 30, 2011; 286(39):33910-20

External Links:

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Image Gallery:

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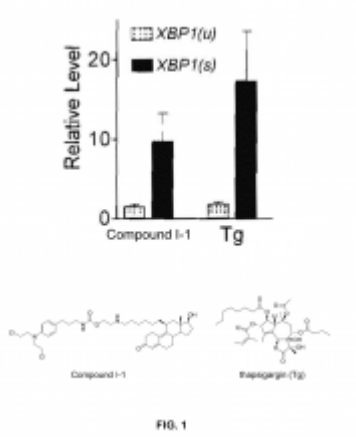

FIG. 1

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