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SMALL MOLECULE INHIBITORS OF CALCIUM-ACTIVATED CHLORIDE CHANNELS TO TREAT SECRETORY DIARRHEA

Tech ID: 18981 / UC Case 2008-060-0

FULL DESCRIPTION

Diarrhea is a major cause of death worldwide, especially in children below five years of age. Chloride channels, such as the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) and Calcium Activated Chloride Channels (CaCCs) play various roles in different types of diarrheas. CaCCs are thought to mediate diarrhea that occurs as a side-effect of certain therapies (i.e. chemotherapy or antiretroviral therapy) or as a result of viral infection. Small molecule inhibitors of intestinal CaCCs are predicted to be useful for treating some types of secretory diarrhea. However, CaCC inhibitors currently available are non-selective and non-potent for blocking CaCC activity.

DESCRIPTION: Using a high-throughput, phenotype-based screen, UCSF investigators have identified two novel chemical classes (aminothiophenes and aminothiazoles) of small-molecule inhibitors of human intestinal CaCC. Using in vivo and in vitro assays, the investigators determined that these inhibitors are specific and likely to target the CaCC directly to modulate gating. The compounds have been synthesized de novo and their structures verified. Structure-Activity Analysis pinpointed the functional chemical groups responsible for inhibitory activity. The investigators envision these compounds could be developed further for treatment of certain types of secretory diarrhea where CaCCs play a role.

FEATURES/BENEFITS

- ▶ The inhibitors are specific for CaCC in human intestinal cells and likely directly affect channel gating

APPLICATIONS

- ▶ These inhibitors represent a novel treatment approach for certain types of diarrhea and could potentially be used in combination with other drugs, such as CFTR inhibitors

REFERENCES

De la Fuente R., et al. Mol Pharmacol. 2008 Mar;73(3):758-68. Epub 2007 Dec 14. Small-molecule screen identifies inhibitors of a human intestinal calcium-activated chloride channel.

CONTACT

Todd M. Pazdera
todd.pazdera@ucsf.edu
tel: 415-502-1636.



OTHER INFORMATION

KEYWORDS

diarrhea, secretory diarrhea, CaCC

CATEGORIZED AS

- ▶ Medical
- ▶ Disease: Digestive System
- ▶ Therapeutics

RELATED CASES

2008-060-0

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	9,789,095	10/17/2017	2008-060

ADDRESS

UCSF

Innovation Ventures

600 16th St, Genentech Hall, S-272,
San Francisco,CA 94158

CONTACT

Tel:

innovation@ucsf.edu

https://innovation.ucsf.edu

Fax:

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