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# Small Molecule Pendrin Inhibitors for Treatment of Inflammatory Airway Diseases and Diuretic Resistance

Tech ID: 29595 / UC Case 2016-154-0

## INVENTION NOVELTY

Small molecule pendrin inhibitors for treating inflammatory lung diseases.

## VALUE PROPOSITION

Cystic fibrosis (CF) is a life-limiting disease, affecting several organs including lungs, kidneys and intestine. Among the severe symptoms, lung infections are responsible for death in 80% of the patients. Most current therapies for CF rely on mucolytics or inhaled antibiotics. Medications such as ivacaftor target only a small subset of CF patients due to the well-defined genetic mutations causing CF. Therefore, a general drug therapy that could potentially alleviate symptoms in all CF patients would be very valuable.

Pendrin (*PDS*, *SLC26A4*) is a sodium-independent chloride and iodide transporter, expressed in the epithelium of inflamed airways. By alerting the airway surface liquid (ASL), a tightly regulated liquid layer that is instrumental in protecting the lung against infection, pendrin has been implicated to be the cause of the progression of inflammatory lung diseases in CF patients. Therefore, pendrin can be a therapeutic target for ASL rehydration. Currently, the best previously described compound for blocking pendrin activity, niflumic acid, produces less than 40% of inhibition and has poor potency with IC<sub>50</sub> of 100 μM. Better molecules are needed to facilitate the development of potential therapies for human diseases.

### ADVANTAGES OF THE INVENTION:

- ▶ Potent inhibitors of pendrin: **IC<sub>50</sub> of 2.5 μM**
- ▶ **Significantly increase ASL hydration** in IL-13-treated HBE and CFBE cell cultures
- ▶ **Highly-specific inhibition of pendrin** compared to other ion transporters

## TECHNOLOGY DESCRIPTION

Researchers in the Verkman lab at the University of California, San Francisco used a high-throughput screen of over 36,000 synthetic small molecules to identify potent inhibitors of human pendrin. Structure-activity studies were performed using primary cultured airway epithelial cells obtained from non-CF (without significant airway diseases) and CF humans. These compounds successfully achieved reversible inhibition of pendrin-mediated anion exchange with an IC<sub>50</sub> of 2.5 μM. Treating airway epithelial cell cultures with PDSinh-A01, increased ASL depth by 8 μm, showing that pendrin inhibition enabled ASL hydration.

## CONTACT

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## INVENTORS

- ▶ Cil, Onur
- ▶ Haggie, Peter M.
- ▶ Verkman, Alan S.

## OTHER INFORMATION

### KEYWORDS

Pendrin, Small Molecule,  
Inflammatory Airway  
Diseases, Diuretic  
Resistance, Cystic fibrosis  
(CF)

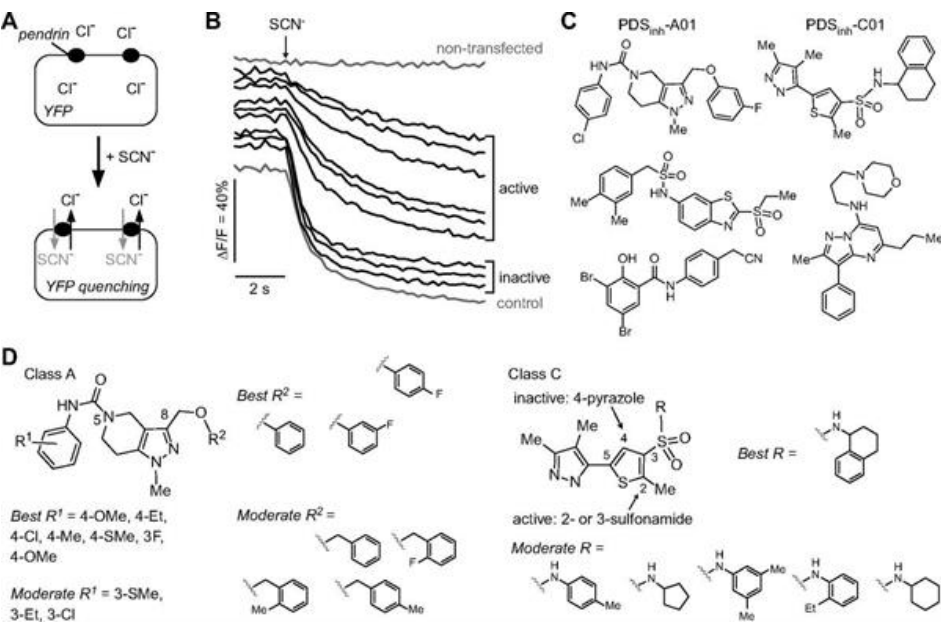
### CATEGORIZED AS

- ▶ **Medical**
  - ▶ **Disease:**  
Autoimmune and  
Inflammation
  - ▶ **Disease: Respiratory  
and Pulmonary System**
  - ▶ **Therapeutics**

### RELATED CASES

2016-154-0

In 35% of the congestive heart failure patients, loop diuretic resistance occurs after taking chronic oral loop diuretics, such as furosemide. A combination treatment of furosemide and 1  $\mu$ M of one of the pendrin inhibitors (PDSinh-C01), resulted in a 60% increase in urine production in a chronically-treated furosemide mouse model, suggesting that in addition of increasing ASL rehydration, these pendrin inhibitors also have the potential as therapies to enhance loop diuretic activity.



LOOKING FOR PARTNERS

To develop and commercialize this technology as innovative therapies for patients with pulmonary, renal, and cardiovascular diseases.

APPLICATIONS

- Oral, parenteral and inhalation formulations of novel diuretics, anti-hypertensives, and expectorants.
- Edema, diuretic-resistant edema, hypertension, asthma, CF, COPD, rhinitis, chronic rhinosinusitis and infection, hyperthyroidism due to thyroid nodules, hyperplasia, thyroiditis.

STAGE OF DEVELOPMENT

Preclinical

RELATED MATERIALS

- [Haggie, Peter M., et al. "Inhibitors of pendrin anion exchange identified in a small molecule screen increase airway surface liquid volume in cystic fibrosis." The FASEB Journal 30.6 \(2016\): 2187-2197.](#)

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	<a href="#">10,702,506</a>	07/07/2020	2016-154
European Patent Office	Published Application			2016-154

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- [CFTR potentiators and correctors and bifunctional \(corrector/potentiator\) compounds for treatment of Cystic Fibrosis](#)
- [SALT-SPARING UREA TRANSPORT INHIBITOR DIURETICS FOR TREATMENT OF CARDIOVASCULAR AND RENAL DISORDERS](#)

- ▶ [Potent TMEM16A Small Molecule Treatment for Inflammatory and Reactive Airway Diseases, Asthma, Hypertension, Pain and Cancer](#)
- ▶ [Novel Small Molecule Drug for the Treatment of Constipation and Oxalate Kidney Stones](#)
- ▶ [Immunotherapy for Treatment of Neuromyelitis Optica \(NMO\)](#)

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