

Covalent Activators Of K₂p Channels

Tech ID: 30178 / UC Case 2017-124-0

INVENTION NOVELTY

Researchers at UCSF have developed a series of small-molecules that selectively label the TREK1 (KCNK2) potassium ion channel. These compounds are the first covalent activator of any member of the K₂P family of potassium ion channels.

VALUE PROPOSITION

Ion channels produce electrical impulses that drive thoughts, moods, movement, and sensation. TREK subfamily of potassium ion channels produce 'leak' currents that stabilize the membrane resting potential, and has a critical role in regulating the activity of excitable cells in the brain, cardiovascular, and sensory systems. The TREK channels have recently been shown to play an important role in electrogenesis, ischemia, anesthesia, mood disorders and pain. TREK1 has therefore emerged as a promising biological target for new neurology and anesthesiology therapeutic agents. However, a lack of effective chemical tools has limited researchers' ability to develop a deep understanding of TREK function and its exact role in disease progression. Researchers at UCSF have identified a novel allosteric pocket unique to the TREK subfamily of potassium ion channels, and developed a series of covalent small-molecule modulators that specifically target TREK1. All members of the series increase TREK1 activity over channel baseline, and their covalence has been confirmed with x-ray crystallography and/or washout studies.

TECHNOLOGY DESCRIPTION

The newly identified chemical probes consist of an aromatic region that specifically binds to a novel allosteric pocket unique to the TREK1 potassium ion channel, as well as an electrophilic moiety that binds to the channel. Treating cells expressing wild-type K₂P or mutant channels with the appropriate electrophile results in 2-5 fold activation of the channel over baseline activity.

LOOKING FOR PARTNERS

To develop and commercialize this technology as a research tool or drug discovery lead. Immediate goals include functionalizing this series of compounds with chemical handles to facilitate attachment of biological probes such as biotin, fluorescent molecules, quantum dots, etc.

RELATED MATERIALS

- ▶ [K2P2.1 \(TREK-1\)-activator complexes reveal a cryptic selectivity filter binding site - 07/20/2017](#)

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- ▶ [Efficient genetic system for high throughput screening of new compounds that modulate activity of potassium ion channels](#)
- ▶ [A Novel Tumor Targeting Strategy for Cancer Chemotherapy](#)
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CONTACT

Ellen Kats
ellen.kats@ucsf.edu
 tel: [View Phone Number](#).



INVENTORS

- ▶ Bryant, Clifford
- ▶ ElHilali-Pollard, Xochina C.
- ▶ Lolicato, Marco GL.
- ▶ Minor, Jr., Daniel L.
- ▶ Renslo, Adam R.

OTHER INFORMATION

KEYWORDS

electrogenesis, ischemia,
 anesthesia, mood disorders, pain

CATEGORIZED AS

- ▶ **Medical**
 - ▶ Disease: [Cardiovascular and Circulatory System](#)

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