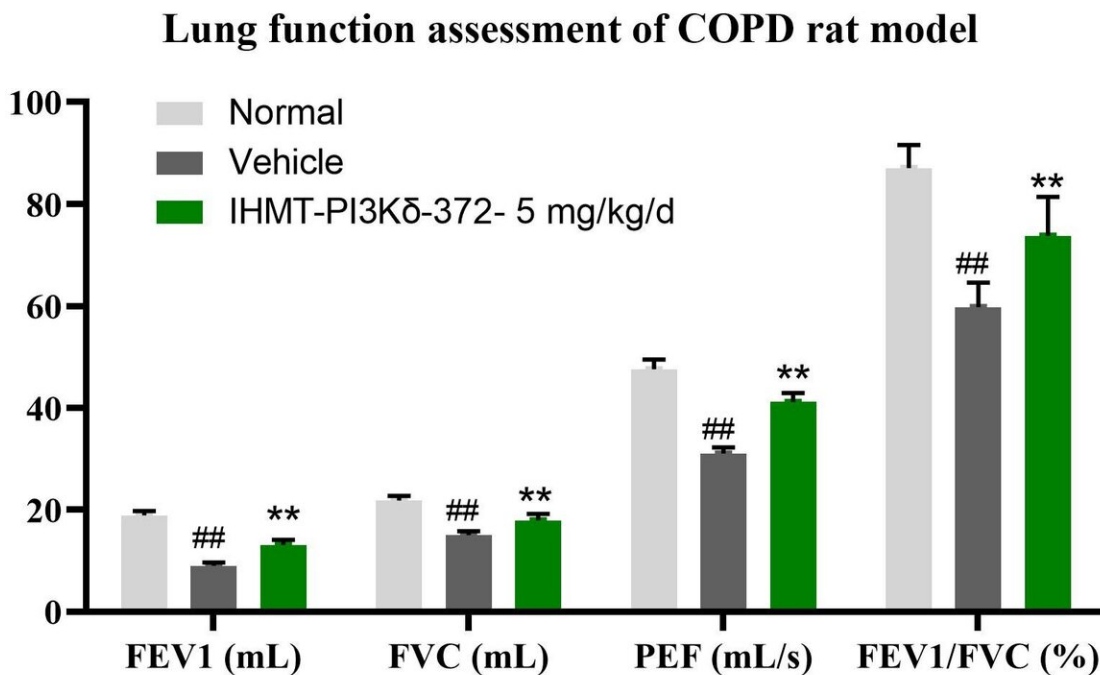


Researchers discover inhibitor for chronic obstructive pulmonary disease

December 3 2020, by Zhang Nannan



In vivo efficacy evaluation of IHMT-PI3K δ -372 in a lung inflammation rodent model. Credit: LI Feng

Recently, a research team led by Profs. Liu Qingsong and Liu Jing from the Institute of Health & Medical Technology of the Hefei Institutes of Physical Science (HFIPS) discovered a potent and selective PI3K δ inhibitor IHMT-PI3K δ -372, effective against chronic obstructive

pulmonary disease (COPD) in vivo.

COPD is a chronic progressive respiratory disease characterized by airflow limitation and associated with abnormal inflammatory response of the lung. In recently years, it is becoming a major health problem and the third cause of death worldwide. Although oral administration of PI3K δ inhibitor is reported to exhibit adverse effects as an [anti-cancer drug](#) in the clinic, inhaled [drug delivery](#) for respiratory disease may result in a potential reduction or avoidance of systemic side effects by delivering drugs directly to the site of action.

In this study, the researchers adopted a fragment hybridization strategy and discovered a novel PI3K δ inhibitor IHMT-PI3K δ -372 through medicinal chemistry exploration.

The compound showed high potency against PI3K δ , and meanwhile exhibited high selectivity over other class I PI3Ks as well as a low risk of hERG-mediated cardiac toxicity. Notably, it displayed favorable pharmacokinetic properties for inhaled delivery and improved lung function in a rodent model of pulmonary inflammation.

These results suggest that IHMT-PI3K δ -372 might be a new potential therapeutic candidate for COPD.

More information: Feng Li et al. Discovery of (S)-2-(1-(4-Amino-3-(3-fluoro-4-methoxyphenyl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)propyl)-3-cyclopropyl-5-fluoroquinazolin-4(3H)-one (IHMT-PI3K δ -372) as a Potent and Selective PI3K δ Inhibitor for the Treatment of Chronic Obstructive Pulmonary Disease, *Journal of Medicinal Chemistry* (2020). [DOI: 10.1021/acs.jmedchem.0c01544](https://doi.org/10.1021/acs.jmedchem.0c01544)

Provided by Chinese Academy of Sciences

Citation: Researchers discover inhibitor for chronic obstructive pulmonary disease (2020, December 3) retrieved 26 June 2024 from <https://medicalxpress.com/news/2020-12-inhibitor-chronic-obstructive-pulmonary-disease.html>

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