Blocking the channel: A pharmacologically active antagonist of the two-pore-domain potassium ion channel K2P9.1 (TASK-3)

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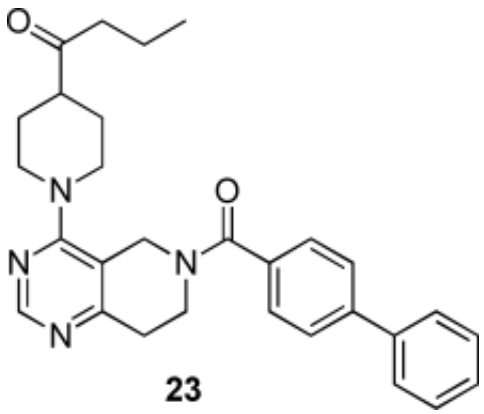

Treatment of neurological conditions such as sleep–wake control, cognition, and depression could be possible by modulation of the TWIK-related acid-sensitive K+ ion channel (TASK-3, or K2P9.1).

A collaborative effort involving scientists at Merck Research Laboratories (USA) and WuXi AppTec (Shanghai, China) led by Craig A. Coburn has identified a new class of potent small-molecule TASK-3 channel blockers through hypothesis-driven screening and a medicinal chemistry lead optimization program, and their results are reported in *ChemMedChem*.

The team profiled one compound in detail and demonstrated central nervous system (CNS) target engagement in rodent electroencephalogram (EEG) telemetry models where compound-induced modulation of quantitative EEG power and sleep architecture appeared absent in knock-out animals that lack this channel subunit. This promising lead compound could prove valuable for further exploration in the challenging field of ion channel modulators.

More information: Craig A. Coburn, Discovery of a Pharmacologically Active Antagonist of the Two-Pore-Domain Potassium Channel K2P9.1 (TASK-3), *ChemMedChem* 2012, 7, No. 1, Permalink to the article: dx.doi.org/10.1002/cmdc.201100351