Metal-Binding Pharmacophore Library Yields the Discovery of a Glyoxalase 1 Inhibitor for Potential Treatment of Depression and Related Psychiatric Illnesses.

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CONTACT

University of California, San Diego
Office of Innovation and Commercialization
innovation@ucsd.edu
tel: 858.534.5815.

OTHER INFORMATION

KEYWORDS

depression, anxiety, epilepsy, alcoholism, blood–brain barrier, psychiatric disorders, therapeutic inhibitor

CATEGORIZED AS

- **Medical**
  - Disease: Central Nervous System
  - New Chemical Entities, Drug Leads

RELATED CASES

2020-039-0

BACKGROUND

Anxiety and depression are the two most common psychiatric disorders in the U.S. and affect approximately one-in-five adults at some point in their lifetime. Depression is the leading cause of worldwide disability; anxiety disorders are highly comorbid with depression. Presently, there are several drugs approved by the U.S. Food and Drug Administration for the treatment of both anxiety and depression; however, these drugs have several important limitations. Antidepressant drugs are not effective in all patients, take weeks to produce therapeutic effects, and produce side effects that limit their use. Anxiolytic drugs produce sedating side effects and have significant abuse liability. Therefore, there is an urgent need for better therapeutic agents. Recent studies using both genetic and pharmacological techniques have implicated GLO1 in numerous behaviors, including several that are relevant to depression and anxiety.

TECHNOLOGY DESCRIPTION

Researchers at UC San Diego have developed glyoxalase (GLO) modulators and methods for treating anxiety, depression, epilepsy, alcoholism, and other forms of drug abuse in a patient and the associated methods for administering to the subject in need thereof a therapeutically effective amount of a compound. Specifically, the inventors have identified novel molecules that inhibit the enzyme GLO1, which is a Zn2+ -dependent isomerase involved in the detoxification of the glycolytic byproducts methylglyoxal (MG). Methylglyoxal (MG) is a reactive metabolite generated via the degradation of glycolytic intermediates and is capable of forming covalent adducts with proteins and nucleotides that result in advanced glycation end (AGE) products, reactive-oxygen species, and apoptosis.

APPLICATIONS

A method for treating anxiety or depression in a subject in need of treatment and a method of administering to the subject in need thereof a therapeutically effective amount of inhibitor.

ADVANTAGES

The newly developed compounds are highly potent GLO1 inhibitors; GLO1 is not currently targeted by any FDA approved drugs. Antidepressant effects can be observed within a few hours in preclinical models that can discriminate between conventional (slow onset) antidepressants like SSRIs and fast acting antidepressants like ketamine. GLO1 inhibitors are not expected to have the abuse liability that limits the use of ketamine.

STATE OF DEVELOPMENT

Animal studies in mice demonstrated that use of the inhibitor produced elevated brain MG levels and produced behavioral changes that are consistent with antidepressant effects. Additional preclinical data relevant to anxiety, epilepsy and alcohol intake / alcohol use disorder are also available.

INTELLECTUAL PROPERTY INFO

The invention is patent-pending and is available for licensing and collaborations

RELATED MATERIALS

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PATENT STATUS

Patent Pending

University of California, San Diego
Office of Innovation and Commercialization
9500 Gilman Drive, MC 0910, ,
La Jolla,CA 92093-0910

Tel: 858.534.5815
innovation@ucsd.edu
https://innovation.ucsd.edu
Fax: 858.534.7345