



TECHNOLOGY

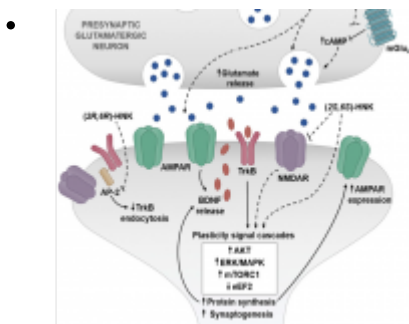
Novel Ketamine Metabolites for Treating Depression, Anxiety & Addiction

OVERVIEW

UMB inventors from Prof. Todd Gould's lab, along with their collaborators, made the pivotal discovery in 2016 that certain stable ketamine metabolites exerted antidepressant actions via a different mechanism (independent of NMDAR inhibition), which made these compounds excellent drug candidates, without the negative side effects associated with ketamine therapy (Zanos et al., 2016 Nature). Their discovery led to a Phase I clinical trial (ID# NCT04711005) currently ongoing to test the safety and pharmacokinetics of antidepressant drug candidate (2R,6R)-hydroxynorketamine, administered by IV infusion to healthy volunteers.

In their continuing laboratory studies of the properties of ketamine metabolites (i.e., 12 unique hydroxynorketamines or HNKs), the inventors observed an association between the 3-dimensional structures of compounds and their relative potencies to induce antidepressant-relevant behavioral effects in the forced swim test in male mice. The inventors synthesized & tested further compounds to explore their structure-activity hypothesis, including (5R)-methyl-(2R,6R)-HNK, which exhibited promising antidepressant-like potency. UMB (in collaboration with NIH) is pursuing patent protection for composition of novel small molecules and their method of use for treating depression, anxiety, addiction, and related disorders.

PHOTOS



APPLICATIONS

Major depressive disorder is common, affecting about 16% of the world population at some point in their lives, and is associated with serious health and socioeconomic consequences. Current pharmacotherapies require prolonged administration (weeks if not months) for clinical improvement. This lag time, as well as a high non-response rate, emphasizes the need for better antidepressant medications. Ketamine has demonstrated rapid and robust efficacy as an antidepressant by improving core depressive symptoms including depressed mood, anhedonia, and suicidal thoughts in treatment-refractory unipolar and bipolar depressed patients when administered at sub-anesthetic doses. However, its potential for widespread clinical use is limited owing to its abuse liability and capacity to produce dissociative effects even when administered at low doses. There remains a critical need for novel, potent drug candidates for the treatment of depression, as well as addiction and related disorders.

ADVANTAGES

- Novel small molecules
- Predict favorable drug properties
- Inventors with clinical drug development experience

STAGE OF DEVELOPMENT

Published proof-of-concept data available for novel compounds in antidepressant-relevant animal model

LICENSING POTENTIAL

Available for licensing

NC 11/07/22

CONTACT INFO

Office of Technology Transfer
620 W Lexington St., 4th Floor
Baltimore, MD 21201
Email: ott@umaryland.edu
Phone: (410) 706-2380

Additional Information

INSTITUTION

University of Maryland, Baltimore

PATENT STATUS

Patent pending (WO 2022/047256)

LICENSE STATUS

Available for licensing

CATEGORIES

- Therapeutics
- Small molecules

INVESTIGATOR(S)

Todd Gould
Jaclyn Highland
Panos Zanos
Craig Thomas
Patrick Morris

ATTACHMENTS

-  [Download UMB Market Summary TG-2021-015 \(Sept 2022\).pdf](#)

EXTERNAL RESOURCES

- [Hydroxynorketamine Pharmacokinetics and Antidepressant Behavioral Effects of \(2,6\)- and \(5R\)-Methyl-\(2R,6R\)-hydroxynorketamines](#)
- [Hydroxynorketamines: Pharmacology and Potential Therapeutic Applications](#)

- NMDAR inhibition-independent antidepressant actions of ketamine metabolites

TG-2021-015