

Ibrutinib as a potential therapeutic for cocaine use disorder (CUD) (2022-008)

Repurposed medication that can be used to prevent various neurobehavioral and neurotoxic effects of cocaine use.

Market Overview

Ibrutinib utilized as a treatment for cocaine use disorder (CUD) can be used as a neuroprotective effect against cocaine toxicity. According to the National Survey on Drug and Health, almost 1 million people in the United States are affected by CUD and 13% of patients in North American substance-use facilities are treated for CUD. However, there are no current Food and Drug Administration (FDA) approved medications for CUD. Current treatments for CUD rely on behavioral modifications through psychiatric treatment. Clemson University and Emory University researchers have partnered up to uncover the efficacy that Ibrutinib can have in targeting and reversing the expression of cocaine addiction genes in human meso-cortico-limbic circuitry. It additionally has been found to significantly reduce incidence of cocaine-induced seizures.

Technical Summary

Ibrutinib has been shown to prevent various neurobehavioral and neurotoxic effects of cocaine use. It is a covalent inhibitor of Bruton's tyrosine kinase and influences intracellular cascades involved in the pro-inflammatory response, Ca²⁺ signaling, and protein kinase activity. These processes are also involved in cocaine use and cocaine-induced seizures. This principle was tested utilizing the *Drosophila melanogaster* model to evaluate its effects on cocaine-induced phenotypes. The *Drosophila* dopamine transporter contains a binding site that can accommodate cocaine and exposure to cocaine gives rise to motor responses that resemble behaviors observed in rodents. In addition, flies express an ortholog of Bruton's tyrosine kinase, BTK29A, in the central brain. Startle behavior and the prevalence of seizure activity was measured in male and female flies following acute consumption of solid food, solid food supplemented with cocaine, or solid food supplemented with cocaine and Ibrutinib. It was observed that both male and female flies that consumed Ibrutinib with cocaine spent more time moving than flies that only consumed cocaine. Male flies that consumed Ibrutinib and cocaine showed a significant decrease in the prevalence of seizures. Fewer cocaine-induced seizures were also observed in Ibrutinib-treated females, but this observation did not reach statistical significance since the incidence of cocaine-induced seizures was lower in females than in males.

Application

Cocaine use disorder, drug addiction, therapy, Ibrutinib, repurposed drug development, biomedical

Development Stage

Proof of Principle

Advantages

- Acts on central brain structures, counteracting neurological pathways for CUD seizures and addictiveness
- Reverses patterns of cocaine gene expression, allowing for CUD psychosocial intervention techniques to become more effective
- Ibrutinib is already an FDA-approved medication for chronic lymphocytic leukemia, making it an optimal option for CUD treatment, which currently has no FDA-approved medication

App Type	Country	Serial No.	Patent No.	CURF Ref. No.	Inventors
Proof of principle	United States	63/071,596	NA	2022-008	Dr. Robert Anholt Dr. Trudy Mackay

About the Inventors



Dr. Robert Anholt

Provost Distinguished Professor of Genetics and Biochemistry at Clemson University

Dr. Robert Anholt is the Provost Distinguished Professor of Genetics and Biochemistry and Director of Faculty Excellence in the College of Science at Clemson University. He earned his Ph.D. in Biology from the University of California, San Diego. Prior to joining Clemson, he served as founding Director of the W. M. Keck Center for Behavioral Biology at North Carolina State University. Among his many accomplishments, he has been awarded the Fellow of the American Association for the Advancement of Science and received the Alexander Quarles Holladay Medal for Excellence from North Carolina State University. After coming to Clemson, Dr. Anholt and Dr. Mackay's laboratories formally merged to focus on establishing causal relationships between DNA sequence variants and variation in organismal phenotype. His current research focuses on exploiting the *Drosophila* model to gain insights into the genetic risk factors that are associated with environmental exposures and can be translated to human genetics, including sensitivity to alcohol, drugs, such as cocaine and methamphetamine, oxidative stress, and heavy metals.



Dr. Trudy Mackay

Professor of Genetics and Biochemistry at Clemson University

Dr. Trudy Mackay is the Director of the Center for Human Genetics, the Self Family Endowed Chair of Human Genetics, and Professor of Genetics and Biochemistry at Clemson University. She earned her Ph.D. in Genetics from the University of Edinburgh. Prior to joining Clemson, she served as the Distinguished University Professor and Goodnight Innovation Distinguished Chair of Biological Sciences at North Carolina State University. Some of her accomplishments include being a Fellow of the American Association for the Advancement of Science, the American Academy of Arts and Sciences and the Royal Society, a member of the US National Academy of Sciences and the American Philosophical Society, the 2016 Wolf Prize Laureate for Agriculture and the 2018 Dawson Prize recipient, Trinity College, Dublin. Her research focuses on utilizing the *Drosophila* model system to further understanding of the genetic basis of quantitative traits and to identify how variation in individual genes and genetic networks affects quantitative traits.

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