

Methods of making and using dopamine receptor selective antagonists/partial agonists

Summary

A library of novel compounds that selectively bind the dopamine D3 receptor have been designed and characterized extensively. In vivo rodent studies indicate selected lead molecules may be useful to treat drug addiction/dependence.

NIH Reference Number

E-053-2016

Product Type

- Therapeutics

Keywords

- oxycodone, dopamine D3 receptor, drug addiction, dependence, Schizophrenia, Bipolar Disorder, cannabis

Collaboration Opportunity

This invention is available for licensing and co-development.

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Description of Technology

Dopamine is a major neurotransmitter in the central nervous system and among other functions is directly related to the rewarding effects of drugs of abuse. Dopamine signaling is mediated by D1, D2, D3, D4 and D5 receptors. The dopamine D3 receptor is a known target to treat a variety of neuropsychiatric disorders, including substance use disorders (e.g. cocaine and opioid), schizophrenia and depression. Despite extensive efforts, it has proven difficult to identify a lead molecule that selectively binds to D3 receptors (versus D2 receptors, for example), with the desired pharmacological and pharmacokinetic profile. For example, metabolic instability or predicted toxicity has precluded successful translation of previously reported D3R-selective antagonists to clinical use for cocaine abuse.

The library of compounds of this technology is designed to have high affinity and

specificity for the dopamine D3 receptor. Preliminary studies at NIDA indicate that selected lead compounds have promising in vivo activity in rodents, including reduced acquisition to self-administration of oxycodone, inhibition of reinstatement to oxycodone seeking, and ameliorating naloxone-precipitated withdrawal from oxycodone dependence, and that these lead compounds are metabolically stable.

Potential Commercial Applications

- Treatment of Opioid Use Disorders, Schizophrenia, Bipolar Disorder, and of cannabis (Tetrahydrocannabinol, THC) dependence

Competitive Advantages

- Despite extensive efforts to develop D₃ receptor-selective compounds, it has proven difficult to identify a ligand with the desired pharmacological and pharmacokinetic profile for translation to the clinic. The D₃ receptor ligands described herein may be useful to treat a variety of diseases, including opioid use disorders and schizophrenia.

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Development Stage

- Pre-clinical (in vivo)

Publications

A. Newman *et al.* [PMID: 27508895]

Patent Status

- **U.S. Patent Filed:** U.S. Patent Application Number 16/084093, Filed 14 Mar 2016
- **Foreign Filed:** International - Patent Application PCT/US2017/02132
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- **Foreign Filed:** Canada - Patent Application 3017342

Therapeutic Area

- Central Nervous System

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