Discovery of LXR Agonists via Pharmacophore Space Mining

https://www.neurodegenerationresearch.eu/survey/discovery-of-lxr-agonists-via-pharmacophore-space-mining/

Principal Investigators

LANG, CHRISTIAN ALEXANDER

Institution

ACELOT, INC.

Contact information of lead PI
Country

USA

Title of project or programme

Discovery of LXR Agonists via Pharmacophore Space Mining

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

204885.3211

Start date of award

15/09/2016

Total duration of award in years

1

Keywords

Acquired Cognitive Impairment... Aging... Alzheimer's Disease... Alzheimer's Disease including Alzheimer's Disease Related Dementias (AD/ADRD)... Behavioral and Social Science... Biomedical Informatics Research... Biomedical Information Resources and Informatics Research... Biotechnology... Brain Disorders... Dementia... Networking and Information Technology R&D... Neurodegenerative... Neurosciences... Translational Research

Research Abstract

The goal of this proposal is to discover drug-like liver X receptor (LXR) ? selective agonists that can halt and reverse the progression of Alzheimer’s disease (AD). Recent work demonstrated

that activation of the LXR signaling pathways leads to improved amyloid ? (A?) turnover, reduction in A? plaque area, and the reversal of cognitive, social and olfactory deficits. The research plan consists of two steps. The first step is computer-aided prediction of agonistic LXR? selective binding, blood brain barrier permeability, and absence of side effects such as mutagenicity or binding to undesired targets. This step relies on a novel method for pharmacophore analysis by examining the joint space of chemical compounds, targets, and chemical/biological properties. This joint space is defined using machine learning on the 3D geometry of spatial arrangement of pharmacophoric points, using attributes such as donors, acceptors, aromatic rings, and charged fragments. The second step consists of biological assays to assess toxicity, brain penetration potential and the ability to induce expression of the corresponding genes. A dozen diverse compounds will have been tested through two iterations of the two steps of in silico prediction and assays at the end of Phase 1. These initial leads will be augmented with additional de novo compounds and further scrutinized via behavioral assays, dose-response studies and more detailed, sophisticated, and mechanistic assays during Phase 2. The outcome of this study will be new drug leads to potentially treat and prevent AD at different stages of cognitive decline and neurodegeneration.

Further information available at:

Types:
Investments < €500k

Member States:
United States of America

Diseases:
N/A

Years:
2016

Database Categories:
N/A

Database Tags:
N/A