

>>>GSK3 β - Small molecule drug leads for Type II Diabetes, Alzheimer's Disease, and Stroke.

>>>market opportunity

Collectively, type II diabetes, Alzheimer's disease, bipolar disorder and stroke have a combined market place in the USA of about US\$10 billion per year.

The development of novel, and effective, drugs to target one or more of these diseases, would help alleviate some of this economic burden by ameliorating the disease and its deleterious sequelae, or delaying the onset of the disease.

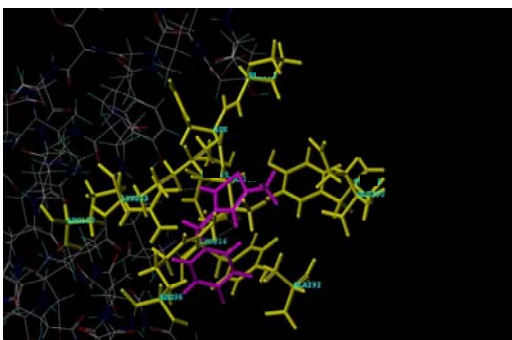
It is estimated that delaying the onset of Alzheimer's disease for five years, from 2005 until 2020, would result in cumulative savings of \$13.5 billion.

>>>project description

Computer-aided, structure-based, molecular modelling is being employed to design novel, small drug molecules that specifically inhibit glycogen synthase kinase 3 β GSK3 β .

GSK3 β is a multifunctional enzyme that is involved in many different metabolic processes, and signalling pathways, including: glucose metabolism, gene expression, cell survival (apoptosis), neuronal structure, and tumour formation. The action of GSK3 β is directly related to its interaction with, and phosphorylation of, metabolic proteins, cell signalling proteins, structural proteins, and transcription factor proteins.

High levels of GSK3 β activity have been implicated in the pathology of diseases including: Type II diabetes, Alzheimer's Disease (and related neurological disorders), and stroke



The innovation of this project comes from the combination of two approaches

(1) Modelling putative binding site pharmacophores, using two complementary strategies, from the structure of GSK3 β .

(2) Generating small molecule leads based on these pharmacophores and then optimising the small molecules using binding potency and 'drug likeness' simulations.

These approaches will produce molecules that will have the required characteristics of good drug leads and also reduce both the time and cost of drug design.

The output of this project will be novel small molecule inhibitors of GSK3 β non-ATP competitive with the significance being effective treatments for Type II diabetes, Alzheimer's Disease, bipolar disease, and stroke.

>>>competing technologies

Inhibitors of GSK3 β are known and most are competitive inhibitors of the ATP binding site within GSK3 β . ATP competitive inhibitors with greater selectivity to GSK3 β have been reported, but most are not selective against GSK3 β and can affect other protein kinases.

This could lead to deleterious side effects if the inhibitors were subsequently used as a treatment. Recently, however, potent non-ATP competitive inhibitors of GSK3 β , based on small heterocyclic thiadiazolidinones (TDZD), have been reported which would potentially help improve selectively and reduce side effects.

>>>intellectual property

Currently there are no patents applied for from the project. Upon creation, early licensing of the technology in the discovery cycle is favoured.

>>>further information

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