CALIFORNIA STATE SCIENCE FAIR
2012 PROJECT SUMMARY

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Project Number
S1724

Project Title
Anti-Alcohol Effects of Ivermectin Analogs on P2X4 Receptors

Abstract

Objectives/Goals
In the US alone, alcohol disorders affect over 18 million people and cause 100,000 deaths annually. Despite this significant social and economic impact, there are only a few treatment options for alcohol abuse and dependence that have yielded only minimal positive outcomes.

Methods/Materials
ATP-gated purinergic P2X4 receptors (P2X4Rs) are a member of the P2XR superfamily and are widely expressed in the brain. P2X4Rs are the most ethanol-sensitive subtype identified to date, when tested in vitro. Recent investigations suggest that P2X4Rs play a role in modulating alcohol consumption in rodents. Ivermectin (IVM - member of the avermectin family) is widely used as an antiparasitic medication in humans and is recognized as a valuable pharmalogical tool for identifying the contribution of P2X4Rs in ATP-mediated processes. Recent in vitro studies in our laboratory found that IVM competitively antagonized the inhibitory effects of ethanol in P2X4Rs.
Our current study starts to investigate the anti-alcohol potential of IVM-like compounds NAP-(1801-1803) using the in vitro screen of P2X4Rs. For this end, P2X4Rs were expressed in Xenopus oocytes and the effects of these compounds on ethanol inhibition was investigated using two- electrode voltage clamp electrophysiology.

Results
Among the few compounds we have tested, NAP-1801 has shown comparable modulating ability and anti-alcohol potential. However, 1802 and 1803 have not.

Conclusions/Discussion
Our studies have led to the conclusion that the ability of IVM/IVM-like compounds to antagonize ethanol inhibition depends on their potential to modulate P2X4R function. Differences in the potential to modulate and/or antagonize ethanol effects in P2X4Rs may be useful in the search for a lead therapeutic agent against alcohol-use disorders.
In the future, we will screen new NAP-compounds for their anti-alcohol potential.

Summary Statement
The anti-alcohol potential of IVM-like compounds (NAP compounds) may be useful in the search for a lead therapeutic agent against alcohol-use disorders.

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