Treatment of Fragile X Syndrome Using Nutlin-3

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The Wisconsin Alumni Research Foundation (WARF) is seeking commercial partners interested in methods for treating the cognitive deficits associated with Fragile X Syndrome using a MDM2-p53 pathway inhibitor.

OVERVIEW

Fragile X Syndrome (FXS) is the most common form of inherited intellectual disability, affecting 1 in 4,000 males and 1 in 6,000 females. It is characterized by severe learning problems, developmental delay and behaviors associated with autism spectrum disorder.

FXS is caused by a mutation in the fragile X mental retardation 1 (FMR1) gene. Despite the intense interest in FXS, especially as a gateway to understanding autism, the precise mechanisms behind the syndrome remain unclear, and to date there is no FDA approved treatment. The failures of recent FXS clinical trials have forced drug developers to rethink target selection for neurodevelopmental indications.

THE INVENTION

UW–Madison researchers have discovered that Nutlin-3, a candidate antitumor drug, and its derivatives may be useful for treating patients with FXS or other intellectual disability. This is the first time that Nutlin-3 has been shown to inhibit adult neural stem cell proliferation and rescue cognitive deficits in a FXS mouse model.

Nutlin-3 is a small molecule MDM2-p53 pathway inhibitor developed in 2004. The researchers use <10x dosage for FXS compared to the dosage used for cancer treatment.

APPLICATIONS

• Potential treatment for FXS and other cognitive deficit disorders

KEY BENEFITS

• Targeting a cell proliferation pathway in neural stem cells provides the much needed...
specificity for therapeutic application.
- Provides a drug development opportunity in surging market space
- Innovative licensing and/or development terms may be available.

**STAGE OF DEVELOPMENT**

The researchers have demonstrated the mechanism of activation of neural stem cells in FXS and identified MDM2-p53 interaction as critical in the pathogenesis of the syndrome. They have shown that treatment with Nutlin-3 normalizes aberrant neurogenesis and neural stem cell proliferation *in vitro* and in mouse models of FXS.

**ADDITIONAL INFORMATION**

**Tech Fields**
Pharmaceuticals & Vitamin D - Neurological & mental health

**CONTACT INFORMATION**

For current licensing status, please contact Rafael Diaz at rdiaz@warf.org or 608-960-9847.