

### New Therapeutic Approach to Parkinson's Disease

A small molecule hit compound with unique functionalities holds out promise for a disease-modifying treatment of Parkinson's Disease and other neurodegenerative diseases. The invention was made by researchers at the University of Vienna, Department for Structural and Computational Biology.

#### **APPLICATIONS:**

Therapeutic treatment of Parkinson's, Alzheimer's and other degenerative CNS disorders.

#### **KEYWORDS:**

Parkinson's, alpha-synuclein, Lcn2/NGAL, neuroinflammation, neurodegenerative

#### **DEVELOPMENT STATUS:**

Proof of concept *in silico*, *in vitro* and *in vivo* (mouse PD model). Derivative compounds being synthesized and tested. Behavioral studies underway.

#### **IPR:**

Priority application filed November 2015

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#### **BACKGROUND**

There are few new drugs for Parkinson's disease in the pipeline, and most of those are either new formulations of known therapies or directed at treating symptoms. There is a great need to discover novel therapeutics targets and strategies that halt or reverse the progression of the disease. Parkinson's disease is a very complex disorder that progresses through several stages, in which alpha-synuclein aggregates accumulate and spread with toxic consequences. Microglial activation leads to inflammation-mediated dopaminergic degeneration in the brain. Drugs that reduce microglial activation could prevent or reverse neuronal degeneration, with significant and long-lasting effects in affected patients.

#### **TECHNOLOGY**

Using our screening strategy we identified a new class of small molecules that binds simultaneously to monomeric and to membrane-bound alpha-synuclein. Moreover these molecules have a high affinity to Lipocalin 2 (Lcn2/NGAL). Lcn2 is a potent neurotoxic factor secreted by reactive astrocytes. Pilot data for our compound in a chronic progressive model of Parkinson's disease, showed that the hit compound is effective in promoting cortical neuron growth in a chronic mouse model, presumably via affecting the distribution between quiescent (healthy) and reactive (toxic) astrocytes.

This unique double-pronged approach to Parkinson's disease exploiting Lcn2 and alpha-synuclein binding properties in a single molecule can potentially deliver a very powerful therapeutic effect, as evidenced by *in vitro* and mouse data.

#### **BENEFITS**

- Original combinatorial therapeutic approach to Parkinson's disease.
- Novel, dual mechanism of action.
- Impact in neuro-inflammation.
- Effects seen in mouse brain sections suggest a true disease modifying therapy.

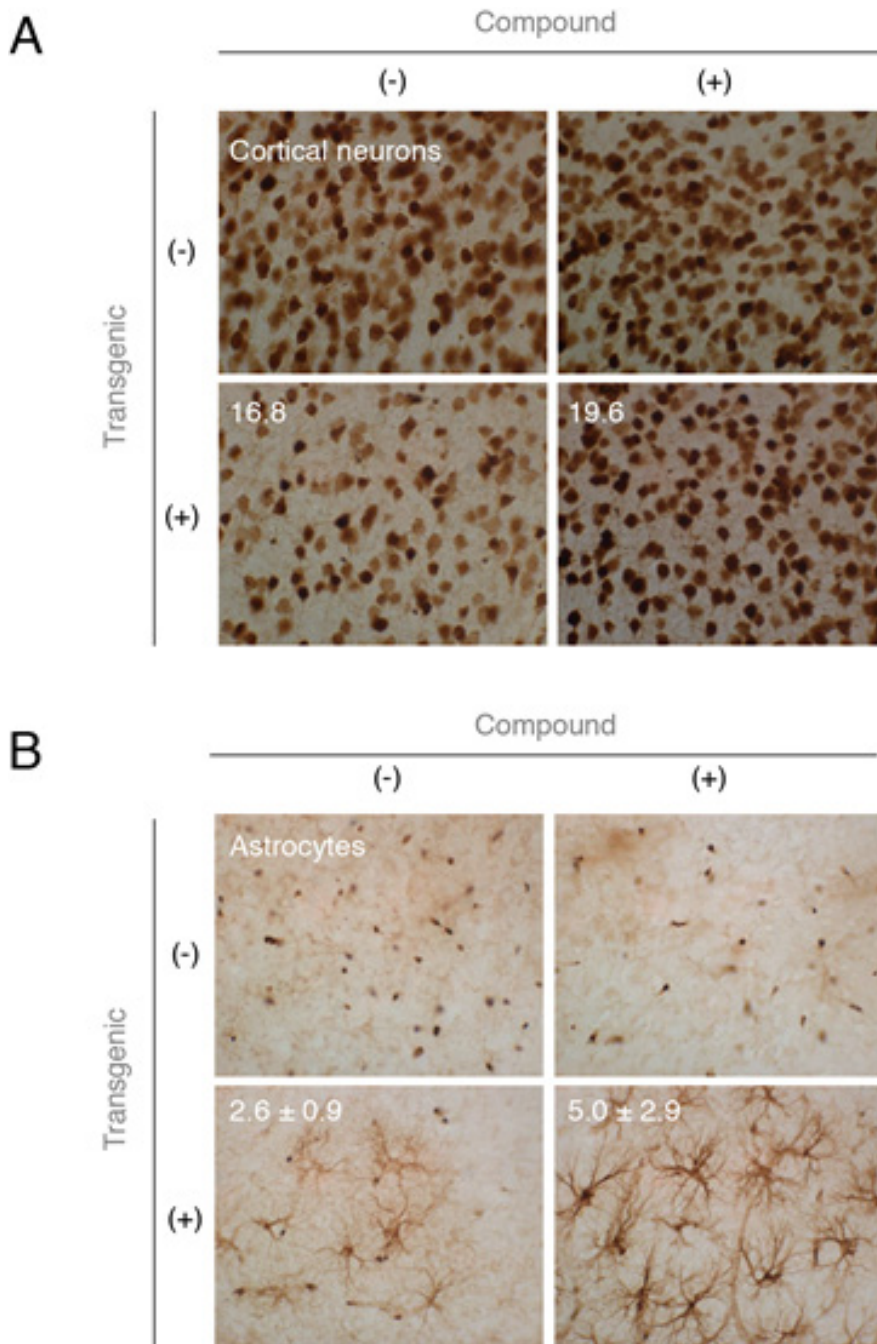


Figure 1. Transgenic PD mice treated with the hit compound of the invention. (A) The compound increases the number of neurons in the cortex of transgenic animal model for Parkinson's disease. (B) The compound increases the astrocyte number in the same mice (bottom right-hand panel).

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