Weill Cornell Medicine

# Non-Invasive Delivery of CNS Gene Therapy Using Focused Ultrasound


**Lead Inventor:**

**Michael G. Kaplitt, M.D., Ph.D.**

Professor of Neuroscience, Brain and Mind Research Institute

Professor of Neurological Surgery



**Business Development Contact:**

Lukasz Kowalik

Senior Licensing and Business Development Officer

(646) 962-7052

kowalik@cornell.edu

# Non-Invasive Delivery of CNS Gene Therapy Using Focused Ultrasound

## Background & Unmet Need

- Gene therapy delivery to the brain is difficult due to the need to cross the blood-brain barrier (BBB)
- Current approaches require the vectors to be introduces through direct injection, which is difficult to monitor and exposes the patient to the risks of invasive surgery
- Use of an osmotic agent such as mannitol enables chemical permeabilization of the BBB but requires systemic administration, precluding targeted delivery
- Administration of MRI-guided focused ultrasound (MRgFUS) has been shown to locally open the BBB, but there is a lack of data demonstrating safe and persistent delivery of therapeutics
- **Unmet Need:** Non-invasive method for targeted delivery of gene therapy to the brain for the treatment of neurological diseases

## Technology Overview

- **The Technology:** Method for transitory disruption of the BBB and targeted delivery of gene therapy using MRgFUS
- Gene therapy delivery can be further restricted by:
    - Encapsulation in vesicles specifically disrupted by FUS
    - Addition of a tissue-specific microRNA to silence off-target gene expression
    - Sequential vector delivery for selective therapy activation
- **PoC Study:** Successfully introduced GFP transgene into the brains of live rats, with stable gene expression up to 16 months after treatment
- Gene expression was shown to be limited to target brain regions and did not provoke long-term inflammation

**Inventors:**
Michael G. Kaplitt
Mihaela Stavarache

**Patents:**
US Application Filed
EP Application Filed

**Publications:**
Stavarache et al. *J Neurosurg.* 2018.

**Biz Dev Contact:**
Lukasz Kowalik
(646) 962-7052
kowalik@cornell.edu

**Cornell Reference:**
D-8560

Weill Cornell Medicine

# Non-Invasive Delivery of CNS Gene Therapy Using Focused Ultrasound

## Technology Applications

- Treatment of neurodegenerative diseases, such as Alzheimer's disease and Parkinson's disease
- Treatment of other CS diseases including major depression
- Treatment of monogenic CNS diseases via gene replacement therapy

## Technology Advantages

- Enables targeting of specific brain regions
- Demonstrated stable gene expression over time
- Increased efficiency and safety compared to current delivery methods

## Supporting Data / Figures

o

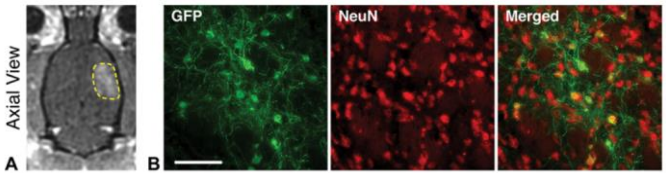


**Figure 1:** MRI-guided focused ultrasound facilitates targeted AAV-mediated gene delivery of GFP to the brain of live rats.

**Inventors:**
Michael G. Kaplitt
Mihaela Stavarache

**Patents:**
US Application Filed
EP Application Filed

**Publications:**
Stavarache et al. *J Neurosurg.* 2018.

**Biz Dev Contact:**
Lukasz Kowalik
(646) 962-7052
kowalik@cornell.edu

**Cornell Reference:**
D-8560

Weill Cornell Medicine


# Weill Cornell Medicine