



# CNS Technologies at the University of Chicago

April 2017

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# CNS Therapeutics

# CNS Therapeutics

## [Awad UCHI 2350](#)

### B-cell Depletion Therapy for Treatment of Rare Neurovascular Disease

- Cerebral cavernous malformations (CCM) are enlarged, brittle blood vessels in the brain that hemorrhage, causing headaches, seizures, paralysis, and hearing or vision loss.
- [Dr. Issam Awad's](#) team has devised a novel treatment, targeting a major mechanism of CCM development, to deplete immune mediating B-cells in order to stop disease progression and new lesion formation.
- This approach would provide a treatment for CCM that is far less invasive than current surgical options which do not prevent development of new CCM lesions.
- Treatment with antibodies against BR3, a B-cell receptor, significantly reduced the development and maturation of brain lesions using a CCM genetic mouse model.
- Nationalization is pending on methods of treating CCM using a B-cell immunomodulation therapy.
- Dr. Awad is designing Phase I clinical trials and seeking commercial partners to continue moving the technology forward through to the clinic.

## [Gomez UCHI 2014](#)

### Novel Approach for Treating Spinocerebellar Ataxia Type 6

- Spinocerebellar ataxia type 6 (SCA6) is a rare genetic disorder in which patients develop loss of coordination, tremors, and uncontrolled muscle tensing. Current therapies address symptoms but not disease etiology.
- [Dr. Christopher Gomez's](#) team has identified a unique target for treatment for SCA6: an internal ribosomal entry site (IRES) in the messenger RNA from the CACNA1A gene which yields a pathogenic product in individuals carrying a gene encoding an expanded polyQ tract.
- A specific microRNA, 3191, can be used for selective translational blocking of the IRES and the treatment of SCA6.
- Delivery of adeno-associated viral microRNA-3191 into SCA6-afflicted mice resulted in selective inhibition of translation from the IRES and alleviated ataxia phenotypes.
- A US application on methods of treatment for SCA6 targeting the IRES and a PCT application on methods of use of microRNA-3191 to treat SCA6 have been filed.
- Dr. Gomez continues to seek new modulators of the IRES. The University is seeking a commercial partner to advance this IRES approach to the clinic.

# CNS Therapeutics

## [Kraig UCHI 2146](#)

### Exosomes for Remyelination in Progressive Multiple Sclerosis

- There is a large unmet need for therapies that restore myelin lost in multiple sclerosis and other demyelinating diseases such as TBI and migraine.
- [Dr. Richard Kraig](#) is developing an innovative remyelination therapy for multiple sclerosis using exosomes.
- Therapeutic exosomes are generated by stimulating dendritic cells in vitro with oxidative stress, such as INF $\gamma$ . INF $\gamma$ -DC-Exos contain critical miRNAs and targeting molecules, and can be lyophilized for storage.
- Intranasal delivery of INF $\gamma$ -DC-Exos enhances brain myelin above baseline in rats and are preferentially taken up by myelin-producing cells. INF $\gamma$ -DC-Exos also restore myelin following demyelination in vitro.
- Patent applications on methods and compositions are pending in the US, EU, Japan, Canada, and Australia.
- The investigators are evaluating the effectiveness of INF $\gamma$ -DC-Exos in rodent models of MS via different delivery routes, and have identified a scalable source of INF $\gamma$ -DC-Exos for clinical trials.

## [Morgan MBL 0015](#)

### Preventing Protein Aggregation: “Molecular Tweezers”

- Protein aggregation is associated with a number of diseases, such as Alzheimer’s, and may be responsible for tissue damage after traumatic brain injury. There are no approved therapeutics that target toxic protein aggregates.
- [Dr. Gal Bitan](#), at UCLA, has developed “molecular tweezers”—small molecules that inhibit the assembly of A $\beta$  proteins. [Dr. Jennifer Morgan](#), at UChicago, has tested CLR01, is a molecular tweezer that can disaggregate amyloidogenic proteins.
- Molecular tweezers may be important for amyloid-related diseases including Alzheimer’s and Parkinson’s disease as well as for spinal cord injury to improve neuronal survival.
- CLR01 decreased synuclein aggregation and increased neuronal survival in a lamprey model of spinal cord injury.
- UCLA holds composition of matter patents on CLR01. UChicago has a pending patent on methods for inhibiting synuclein aggregation for treating amyloid-related diseases.
- Animal studies to further characterize efficacy and pharmacokinetics of the molecule and associated derivatives are underway, as well as experiments to reveal the structure and mechanism of interaction.

# CNS Therapeutics

## [Prabhakar UCHI 1935](#)

### A small molecule, L-PAG, for the treatment of sleep-disordered breathing

- Current treatments for sleep-disordered breathing (apneas) rely on bulky external devices such as continuous positive airway pressure (CPAP) devices which may not be suitable for all patients.
- [Dr. Nanduri Prabhakar's](#) team has discovered that blocking cystathionine- $\gamma$ -lyase enzyme activity using L-propargylglycine (L-PAG) reduces the aberrant hydrogen sulfide levels that attribute to sleep apneas and returns breathing rates to normal.
- Therapeutic administration of the small molecule, L-PAG, would be used to normalize breathing patterns in patients with apneas without requiring the use of a CPAP device.
- In a mouse model of sleep apnea, mice treated with L-PAG had regular breathing rates as measured by plethysmography.
- A US patent application is pending on methods of treating sleep-disordered breathing with L-PAG and its derivatives. A provisional application has been filed on new compositions of L-PAG.
- Dr. Prabhakar and his collaborators are assessing pharmacokinetics and toxicology in preparation for an IND filing.

## [Tian UCHI 2545](#)

### Silicon nanomaterials for the activation of neuronal cells

- Devices for neural stimulation interact with neural tissues at different degrees of precision and invasiveness, resulting in incomplete or inefficient neural stimulation.
- [Dr. Bozhi Tian](#) has engineered amorphous, porous silicon particles with bioelectric activity and softer properties that form to the surface of the cell plasma membrane.
- A therapeutic administration of the silicon material enables the stimulation of neuronal cells upon light activation.
- Generation of a bioelectric currents by light induction of the silicon material was demonstrated using dorsal root ganglia neurons in vitro.
- A PCT application has been filed on the amorphous, porous silicon material.
- Researchers are examining the materials in mouse models for neural and cardiac stimulation.

# CNS Diagnostics

# CNS Diagnostics

## [Cacioppo UCHI 2382](#)

### Analytical Suite for Improved Time-Variied Data Segmentation

- Electroencephalography is a common method to detect problems in the electrical activity of the brain, however, rapid brain transition states are easily missed with current electroencephalogram (EEG) parameters, resulting in unreliable results and missed diagnosis of brain disorders.
- Drs. [Stephanie Cacioppo](#) and [John Cacioppo](#) have designed and applied an analytical suite that analyzes complex, high-density brain electrical signals that can distinguish between stable and transition brain states at specific time points and specific brain locations.
- The software program combines a number of various tools that utilize quantitative methods for robust and automatic detection of event-related changes in global brain activity.
- Researchers have measured EEG readings from human subjects and applied the analytical suite to measure changes in brain activity in response to various stimuli.
- A US application is pending on a non-transitory computer-readable medium to determine the stable states in the subject.
- Drs. Cacioppo are looking for commercial partners to further develop and utilize the EEG analysis suite, and expand its application for other large data set analysis programs.

## [Popko UCHI 2112, 2250](#)

### PET Imaging Agent for Diagnosis and Monitoring of Multiple Sclerosis and Traumatic Brain Injury

- Readout from MRI correlates imperfectly with MS pathology; tools are needed to more accurately assess disease status.
- [Dr. Brian Popko](#) has exploited the exposure of potassium channels upon neuron demyelination as a mechanism by which to visualize the status and progression of MS.
- Derivatives of 4-aminopyridine, which bind to potassium channels, are labeled with an isotope to visualize disease progression or to monitor remyelination during therapy.
- The imaging agent has been demonstrated to highlight demyelination in rodent spines and brains in autoradiography and microPET experiments.
- Applications filed in the US, Europe, Canada, and Australia, with claims issued in the US and Europe, for an imaging agent made of radiolabelled 4-AP or derivatives and uses of the agent for imaging patients with demyelinating disorders.
- The investigators are conducting experiments to test the imaging agent in non-human primates.



# CNS Research Programs

# CNS Research Programs: Neurodegenerative Disease

## Amyotrophic Lateral Sclerosis

[Dr. Raymond Roos](#) has discovered several targets within the unfolded protein response pathway that play a critical role in ALS pathology by enabling aggregation of mutant SOD1. The team is investigating a variety of RNAi and protein-based approaches for modulating this pathway that may have therapeutic potential.


## Parkinson's Disease

[Dr. Xiaoxi Zhuang](#) and colleagues have developed what may be the best mouse model of Parkinson's disease to date. They have also identified a new target for treating Parkinson's disease, adenylyl cyclase type 5. Investigators propose to use AC5 inhibitors to treat PD as a first line therapy and predict that such treatment would restore motor function in Parkinson's patients without inducing dyskinesia.

## Alzheimer's Disease

[Dr. Sangram Sisodia](#) examines the cellular and molecular biology of the amyloid  $\beta$  precursor protein (APP) and presenilins (PS1 and PS2), molecules that are mutated in pedigrees with autosomal dominant, familial forms of Alzheimer's disease. Investigators are characterizing the domain of the gamma-secretase complex that binds APP substrate, facilitating its cleavage to amyloid  $\beta$ .

[Dr. Gopal Thinakaran's](#) lab investigates the cell biology of two proteases - BACE1 and gamma-secretase - which sequentially cleave APP to generate amyloid  $\beta$ . Investigators use cultured neuronal and non-neuronal cell lines, primary neurons, knock out mice and transgenic mouse models of AD pathogenesis in their investigations.



# CNS Research Programs: Autism

## Behavioral Screening Method for Autism

[Drs. Peggy Mason](#) and [Aaron Fox](#) have discovered that several genetic and pharmacological mouse models of autism are particularly sensitive to a common pharmaceutical. They propose a combination of a low dose of the pharmaceutical with a simple behavior test as an autism screening method for children younger than 2 years of age. The investigators are seeking research collaborations to further the validation and development of the screening method.

## Mouse Models of Autism

[Dr. Christian Hansel's](#) lab studies the mechanisms of neuronal plasticity in the cerebellum, which is increasingly appreciated to play a causal role in autism. By using this simple system with well-known and mapped synapses, Dr. Hansel is able to identify whether particular pharmacological or other manipulations have an effect on plasticity, specifically long-term depression, providing a screening method for identifying potential autism therapeutics.



# CNS Research Programs: Neuroprosthetics

## Motor Intention

[Dr. Nico Hatsopoulos's](#) lab uses mathematical models to decipher or “decode” motor cortex activity during behaviors in order to predict the neural activities that generate limb movement. This research has led to successful brain-machine interface technologies and may ultimately allow people with spinal cord injury, ALS, or amputation to use brain signals to control a prosthetic limb.

## Sensory Perception

[Dr. Sliman Bensmaia's](#) lab studies how sensory information is encoded in nerves and the brain and is developing approaches to convey meaningful and naturalistic sensations through stimulation of peripheral or cortical neurons. The ultimate goal of this work is to create robotic arms that are interfaced directly with the nervous system and which not only respond to commands from the brain's motor systems, but restore touch sensation.

# How to Partner with the University of Chicago

Contact the Polsky Center for Entrepreneurship and Innovation Technology Commercialization and Licensing team and speak to anyone on the project management team.



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