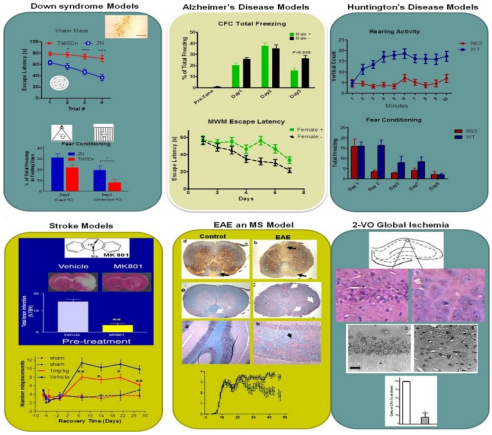
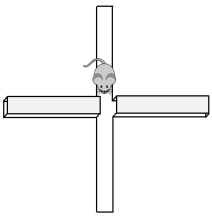
Stanford
MEDICINE

neurobehavior@stanford.edu

2018





Stanford Behavioral and Functional Neuroscience Laboratory (SBFNL)

MISSION STATEMENT

Create a shared resource platform for academic labs, providing access to rodent testing in existing and novel paradigms for characterizing cognition and behavior.
Accelerate progress in both fundamental and applied studies of nervous system function that will serve as a resource to investigation of the normal and the diseased nervous system.

Stanford Behavioral and Functional Neuroscience Laboratory has two locations on the Stanford campus:

SIM1 (Lokey Stem Cell Building) and Arastradero, providing over 5,000 sq. ft. of testing, housing and laboratory space.

The center is operated by a team of experienced Postdoc's and Life Science Research Assistant's.

Stanford Behavioral and Functional Neuroscience Laboratory is supported by a NIH P30 Center Core Grant and the Stanford Neurosciences Institute (SNI).

SIM1 Building

Arastradero Building

GOALS

Stanford Behavioral and Functional Neuroscience Laboratory aims to support and accelerate translational and preclinical neuroscience research through the following collaborations and services:

- Provide state-of-the-art tools
- Provide phenotyping services for novel transgenic lines
- CNS Disease Models
- Neuropharmacology
- Provide an integrated infrastructure for experimental design oversight and data analysis
- Train undergraduate, graduate students and PhD fellows
- Develop and implement new and emerging behavioral technologies



Stanford Behavioral and Functional Neuroscience Laboratory facilities are under a reverse light-dark cycle. This allows us to test rodents during their natural active period.

Being a part of the Behavioral and Functional Laboratory, is an opportunity to participate in some exciting basic and translational research in the field of neuropharmacology and behavioral neurosciences with a focus on brain disorders.

This is a great opportunity for undergraduates considering medical school or current medical students with interest in the translational neurosciences to gain hands-on laboratory and theoretical experience.

We welcome highly motivated postdoctoral fellows and graduate students!

Cognitive Tests:

Learning and Memory:

- Morris water maze
- Delayed-Matching-to-Place water maze
- Barnes maze
- T maze
- Y maze
- Fear conditioning
- Novel object recognition
- Novel location recognition
- Passive avoidance test
- Conditioned place preference

Anxiety:

- Elevated zero maze
- Elevated plus maze
- Light-Dark box

Social Tests:

- Tube dominance test
- 3 Chamber test
- Interaction by pair test
- 5-Trial social memory test
- 2-Trial social memory test
- Automated social test
- Ultrasonic vocalization test

Stanford Behavioral and Functional Neuroscience Laboratory can modify and expand upon existing behavior protocols or design new testing paradigms to best study the behavior you are interested in.

Sensorimotor Tests:

- Open field activity test
- Activity chamber test
- Basket test
- Cylinder test
- Hot plate test
- Grip strength test
- Rota-rod performance test
- Horizontal ladder test
- Paw misplacement test
- Inclined platform test
- Beam walk test
- Garcia neurological test
- Twenty-eight point neurological scoring
- Olfactory test
- Catwalk stride test
- Automated Home Cage activity
- Running Wheel activity
- Pre-pulse inhibition
- IntelliCage

Disease Models:

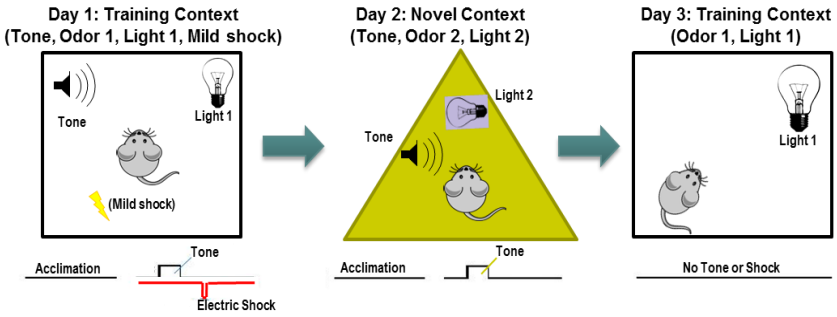
- Alzheimer's disease
- Down syndrome
- Huntington’s disease
- Parkinson’s disease
- Autism
- ALS
- Addiction
- Focal ischemia
- Global ischemia
- EAE
- ICV, and other modes of Delivery
- PK
- PD
- BBB permeability studies
- Non-GLP safety studies

...and many more!

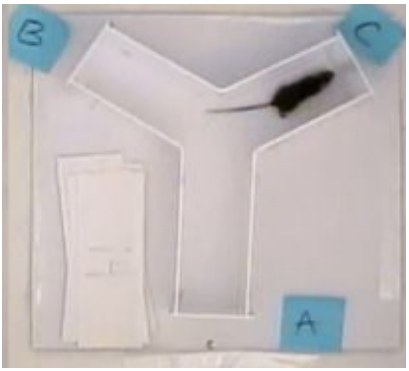
Stanford Behavioral and Functional Neuroscience Laboratory can provide expertise in all aspects related to the design and implementation of behavioral experiments as well as data analysis and interpretation. The core is equipped to accommodate a full battery of behavioral tests relevant to learning and memory, sensory gating, motor function, nociception, and anxiety-related behaviors. Here are some examples of the services we can provide:

Fear Conditioning

Trace Fear Conditioning (FC) is used to assess Pavlovian learning and memory in rodent models of CNS disorders. Subjects learn to associate a neutral Conditional Stimulus (CS; a tone) with an aversive Unconditional Stimulus (US; a mild electrical foot shock) and exhibit a Conditional Response (CR; freezing). After repeated pairings of CS and US, the subjects learn to freeze in response to both the tone and training context. The percentage of freezing during a specified time is reported. FC is a useful test for neurobehavioral and genetic studies on transgenic strains of mice, and for pharmacological studies evaluating the effect of novel chemical entities on cognition.



Y Maze



Y Maze Spontaneous Alternation is a behavioral test for measuring spatial working memory based on the willingness of rodents to explore new environments. Rodents typically prefer to investigate a new arm of the maze rather than returning to one that was previously visited. Many parts of the brain--including the hippocampus, septum, basal forebrain, and prefrontal cortex--are involved in this task. This test is used to quantify cognitive deficits in transgenic strains of mice and evaluate novel chemical entities for their effects on cognition.

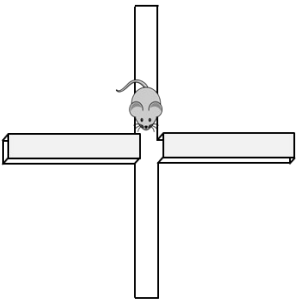
Morris Water Maze

The Morris Water Maze is designed to test spatial memory by observing the subject's ability to find a hidden platform in an opaque water tank.

The subject is trained to use visual cues surrounding the tank to locate the platform. Successful learning of the Morris Water Maze is determined by the gradual decrease in the time it takes to find the platform.

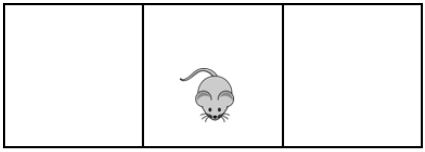
Ethovision Pro(Noldus Information Technology, Wageningen, the Netherlands)

Elevated Plus Maze

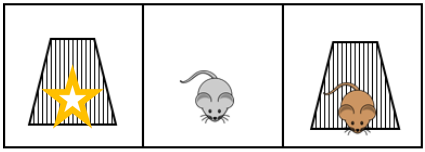


The Elevated Plus Maze test is used to assess anxiety-related behavior in rodent models. The apparatus consists of a "+"-shaped maze elevated above the floor with two oppositely positioned closed arms, two oppositely positioned open arms, and a center area. The subjects freely explore the maze as their behavior is recorded. The preference for being in open arms over closed arms is calculated to measure anxiety-like behavior. This test can be used to phenotype strains of transgenic mice and to screen for putative anxiolytic compounds.

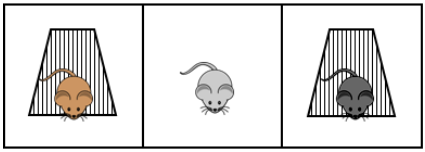
Three Chamber Social Test



Habituation: Empty Apparatus



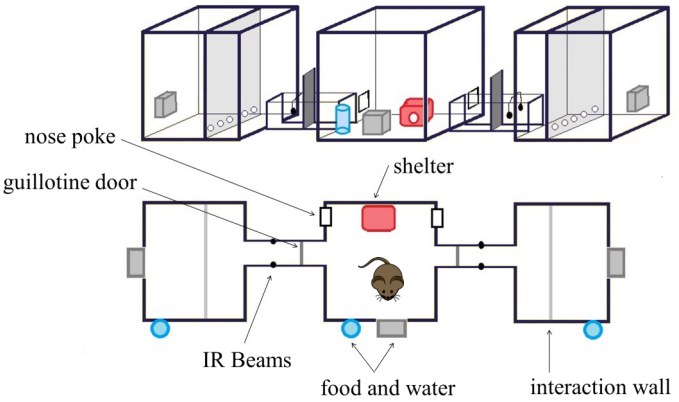
Sociability: Novel Object; Mouse 1



Social Novelty: Mouse 1; Mouse 2

The Three-Chamber test assesses general sociability and interest in social novelty in rodent models of CNS disorders. Rodents normally prefer to spend more time with another rodent (sociability) and will investigate a novel intruder more so than a familiar one (social novelty). Based on these inclinations, the Three Chamber Test can help identify rodents with deficits in sociability and/or social novelty.

Automated Social Test



Sociability: Novel Object; Mouse 1

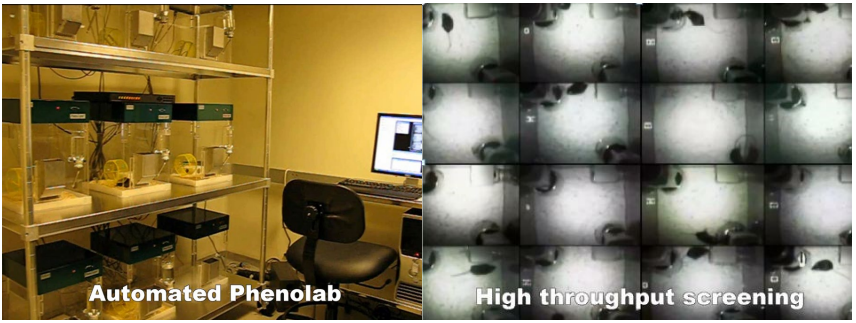
Social Novelty: Mouse 1; Mouse 2

Ethovision XT (Noldus Information Technology, Wageningen, the Netherlands)

The Automated Social Test is a perfect representation of SBFNL's commitment to continually expand and improve upon existing behavioral paradigms. The Automated Social Test takes the ideas behind the Three-Chamber Social Test and allows scientists to expand the test over several days in a home-cage environment with no disruptions from the experimenter. Furthermore, the design of the chambers enables scientists to modify the difficulty of access to interactions by requiring a certain number of nosepokes to open doors to the interaction chambers. This allows us to distinguish between the desire to socialize and mere exploration. No such test of social motivation currently exists, bringing SBFNL to the forefront.

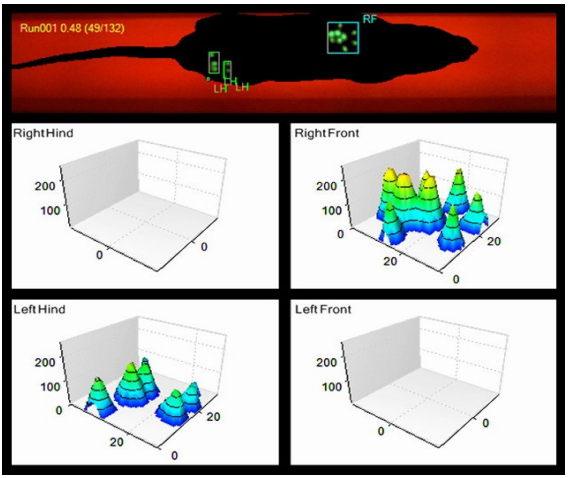
Automated Home Cage Testing

Automated Home Cage testing allows scientists to monitor home cage activity levels and behavior of subjects over several days. The addition of running wheels gives an additional way to assess differences in activity. The Automated Home Cage setup is a high-throughput method for screening subjects after drug treatment or genetic manipulation. Up to 24 cages can be processed at one time.



Ethovision XT (Noldus Information Technology, Wageningen, the Netherlands)

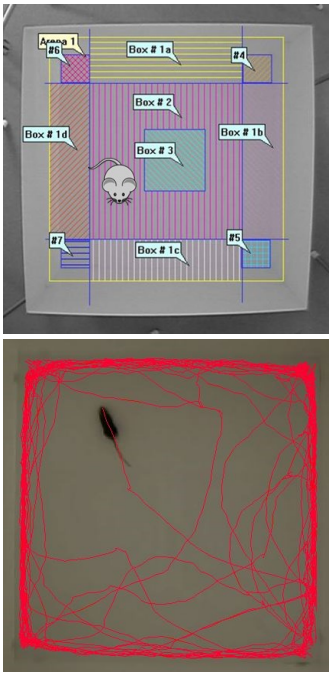
Catwalk



The Catwalk is an automated gait analysis system used to assess motor function and coordination in rodent models of CNS disorders. Subjects walk across an illuminated glass platform while a video camera records from below. Gait related parameters—such as stride pattern, individual paw swing speed, stance duration, and pressure—are reported for each animal. This test is used to phenotype transgenic strains of mice and evaluate novel chemical entities for their effect on motor performance.

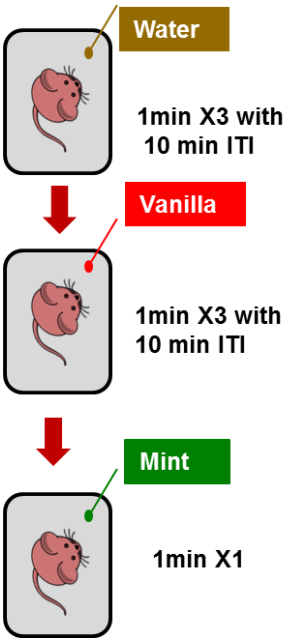
Open Field

The Open Field task is a sensorimotor test used to determine general activity levels, gross locomotor activity, and exploration habits in rodents. The animal is allowed to freely move about a large, square arena for 10 minutes while activity is recorded. The Open Field test is useful for phenotyping transgenic strains of mice and evaluating the effect of novel chemical entities on activity, anxiety, and exploration.



Ethovision XT (Noldus Information Technology, Wageningen, the Netherlands)

Olfactory Test

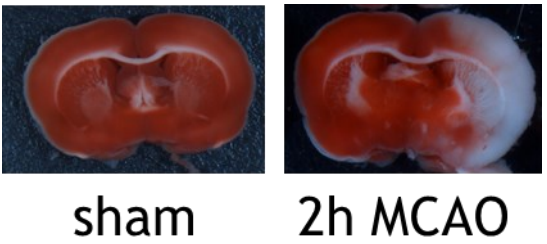


The Olfactory Test is a sensory assay used to measure the olfactory ability, degree of social interest, and perception of social novelty in rodent models of CNS disorders. The nonsocial olfactory test employs water and synthetic odorants while the social olfactory test uses water and urine samples from other animals. Subjects are exposed multiple times to three different odorants and time sniffing the odor is recorded. The olfactory test is useful for evaluating the effect of novel chemical entities and transgenic modifications on olfactory sensation, discrimination, and sociability.

Stanford Behavioral and Functional Neuroscience Laboratory is interested in studying the complex, whole-system effects of disease models and potential treatments. We utilize our expertise in not only BEHAVIORAL testing, but in PHARMACOLOGICAL and DISEASE models to better study neurological disorders and treatments.

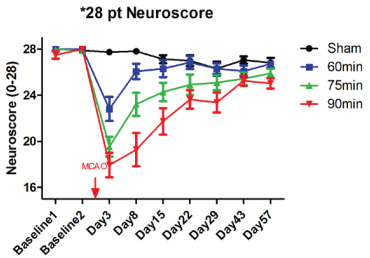
Behavioral testing in tandem with molecular and cellular biology techniques allows us to provide a complete picture of the systems we study. Here is an example of how this merger of information can provide a full story, leading us to significant and exciting discoveries.

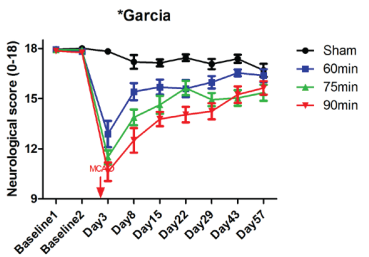
Post-treatment and Neuroprotection in the MCAO Rodent Model of Stroke



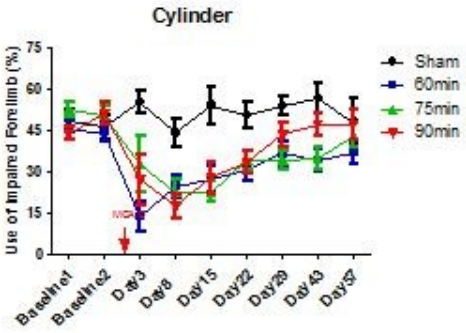
Middle cerebral artery occlusion (MCAO) is a surgically induced cerebral ischemia in rats. In this experiment, we test the efficacy of a drug (CBX) on inducing neuroprotection when given as a post-stroke treatment.

Two main neurological tests are used to assess motor and behavioral deficits in rat models of CNS disorders. Both the Garcia test and the 28 -point Neuroscore test involve a battery of motor tests, ranging from simple observation to traversing a horizontal bar. These tests are well-suited for assessing neurological damage due to ischemia and recovery.





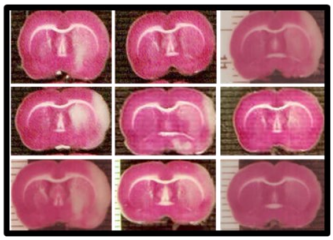
The Cylinder test is designed to evaluate locomotor asymmetry. As the animal moves within an open-top, clear plastic cylinder, its forelimb activity while rearing is recorded. In MCAO rats, the left forelimb is impaired after stroke. Recovery from stroke can be shown by increased use of the impaired forelimb during the cylinder test.



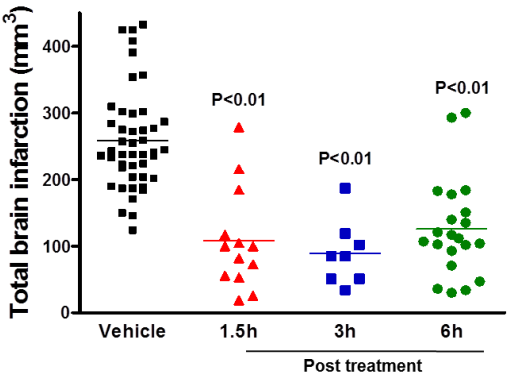
Neuroprotection Achieved by CBX

CBX treatment post-stroke reduces immediate damage to cerebral tissue caused by ischemia.

Vehicle

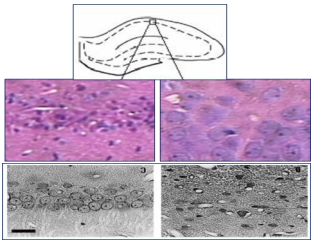


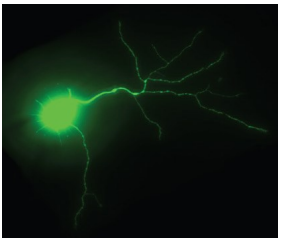
CBX 3 and 7 h



In addition to behavior testing, Stanford Behavioral and Functional Neuroscience Laboratory creates disease models and performs further analysis via biochemical, histochemical, and pathological evaluation of tissues and samples generated from studies.

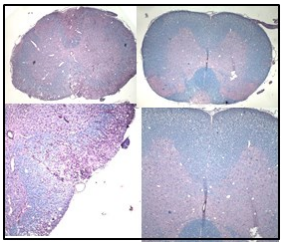
Experimental Stroke Models

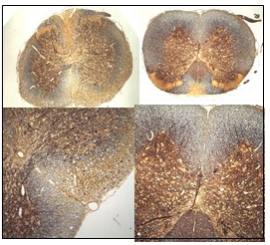


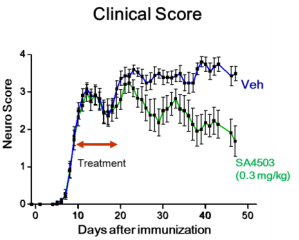


Multiple Sclerosis

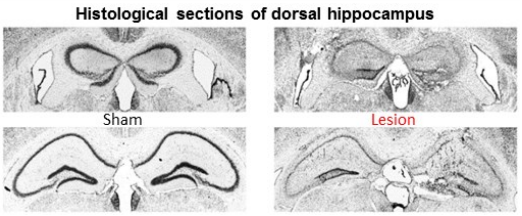
- Experimental Autoimmune Encephalomyelitis (EAE)

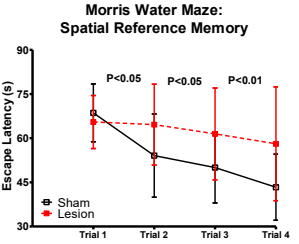






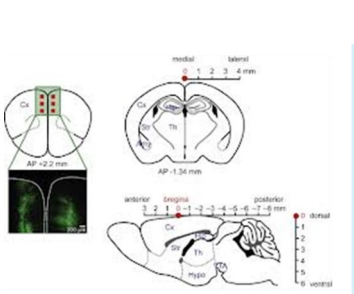
Hippocampal Lesions

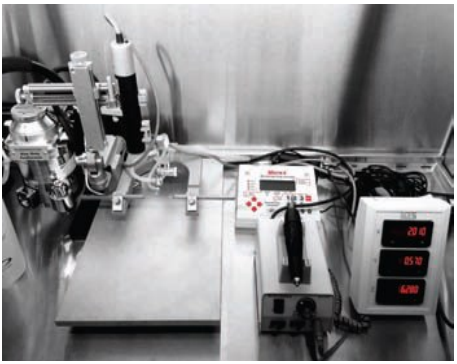




Stereotactic Neurosurgical Procedures

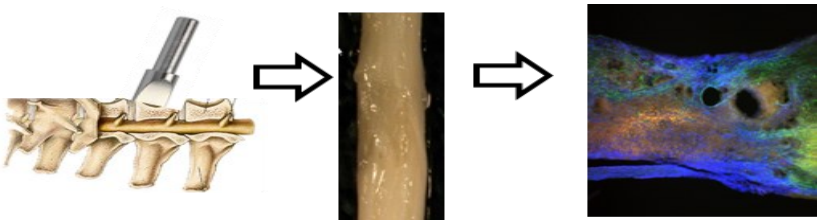
¤Virus and Aβ Injection ¤ Intracranial Injection ¤ Optogenetics
¤Microdialysis ¤ 6-OHDA model of Parkinson's disease



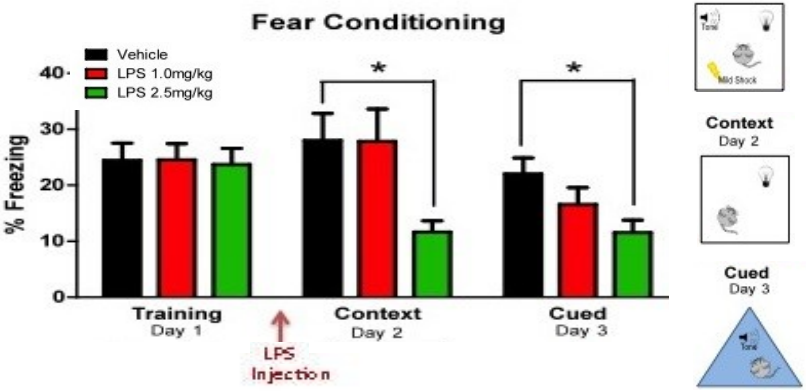


Spinal Cord Injury (Dr. Giles Plant)

- Contusion

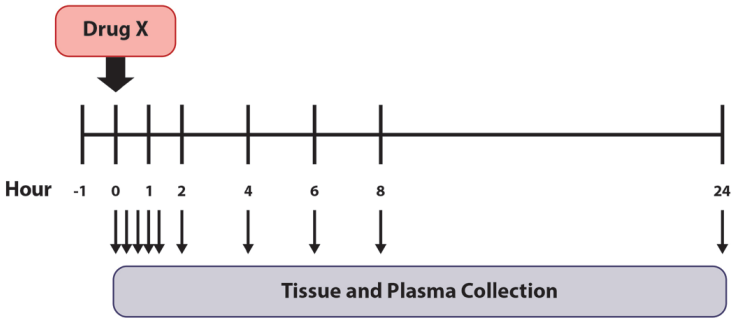


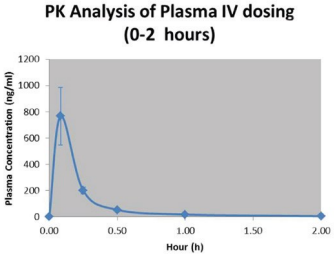
LPS Induced Cognitive Deficits

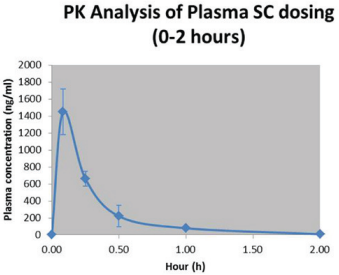


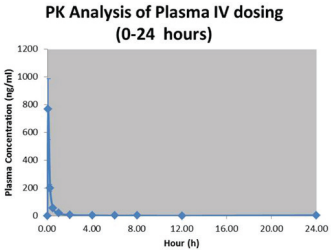
Pharmacokinetic & Pharmacodynamic PK/PD)

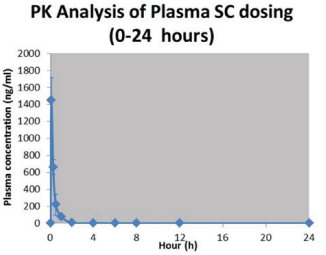
- Bioavailability, biological half-life, elimination rate
- Blood Brain Barrier Permeability
- ICV and other modes of drug delivery

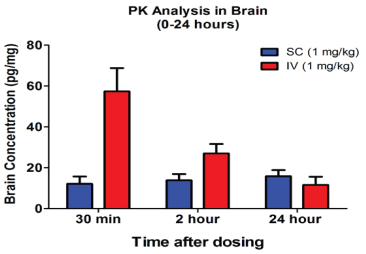






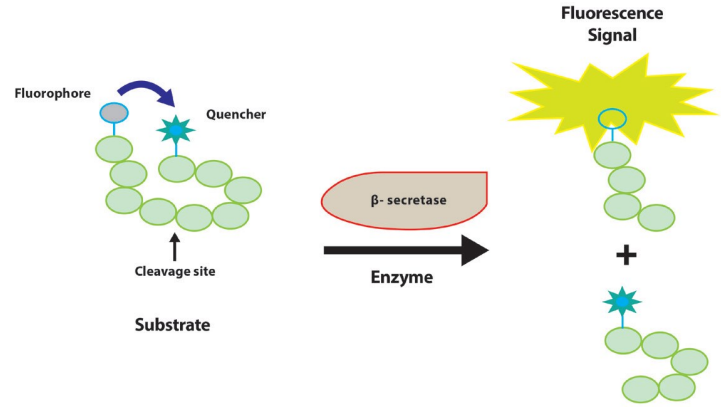


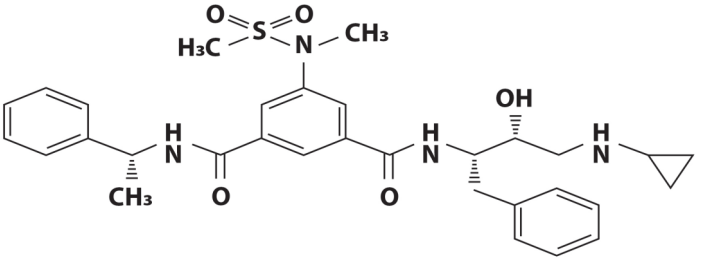




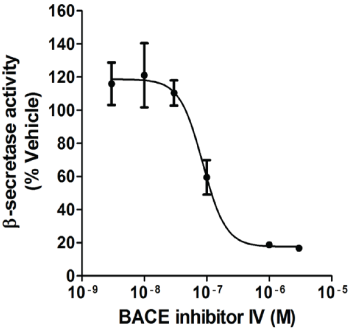
- In Vitro Pharmacology

  •β-secretase assay





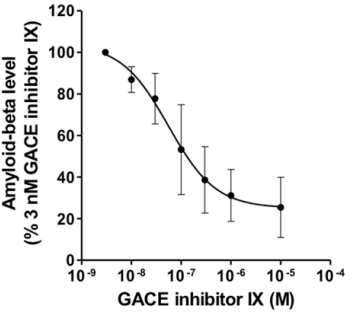
β-secretase is strongly implicated in the pathology of Alzheimer's disease. Thus, modulation of the β-secretase may lead to therapeutic benefits for the treatment of the disease. In this assay, compounds' effects on the activity of β-secretase are tested using the enzyme substrate, which is linked to a fluorophore at one end and to a quenching agent at the other.

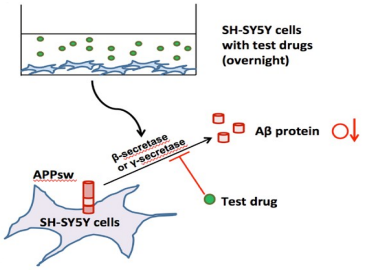


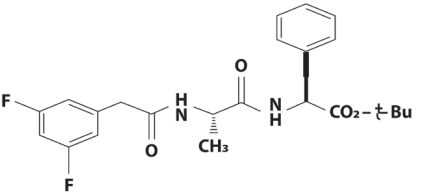
- Cell based Assays

•Amyloid beta toxicity assays

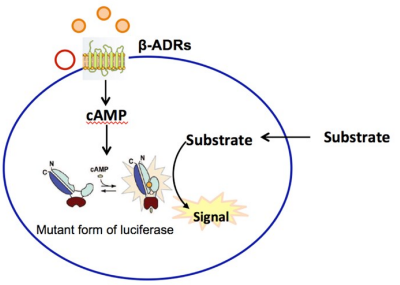
Amyloid peptide (Aβ) has a central role in the pathogenesis of Alzheimer's disease. In this assay, test compounds' effect on the Aβ level are studied using the human neuroblastoma cell line stably expressing Swedish mutant amyloid precursor protein. The levels of Aβ produced with or without test compounds are measured with sandwich ELISA.

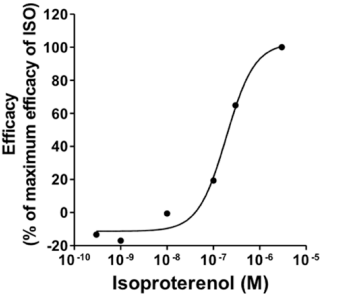




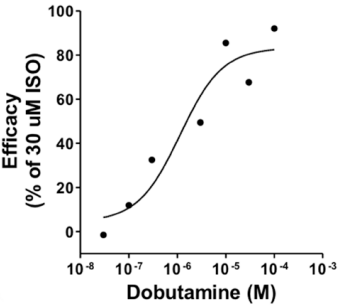


•GPCR (G-protein coupled receptors)





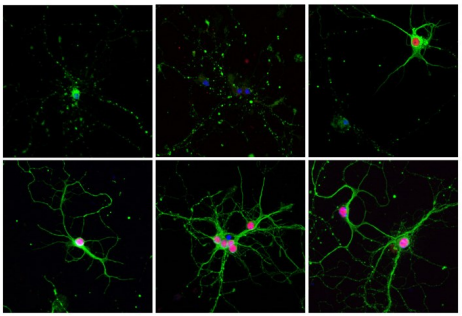
G-protein coupled receptors including adrenergic receptors are one of the most important drug targets. In this assay, effects of test compounds on β-adrenergic receptors are studied using the mutant inactive luciferase, which becomes active in response to cyclic AMP. Activation of the receptor with β-adrenergic receptor agonists lead to the production of cyclic AMP, which in turn increase the level of luminescence signal produced by the luciferase activity.



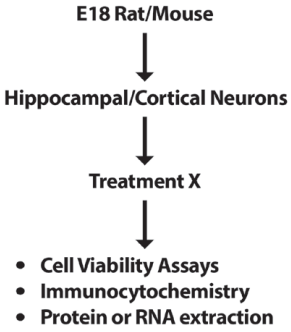
- Primary Cortical Neurons (PCN) and

  Primary Hippocampal Neurons (PHN) Cell Culture

Embryonic hippocampal/cortical neurons are cultured in vitro to study the effect of the drug/treatment on gene or protein expression. The cultured neurons are also useful in studying the morphology of neurons and synapse formation/density. Cell survival and toxicity will be evaluated using different techniques such as western blotting, qPCR, and immunocytochemistry.

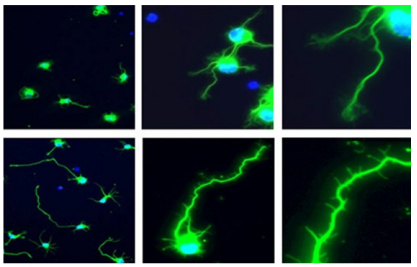


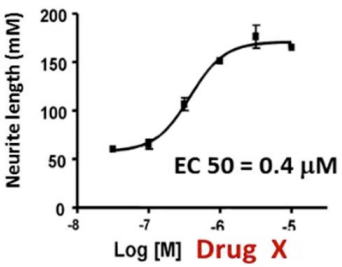
APP Toxicity in PCN

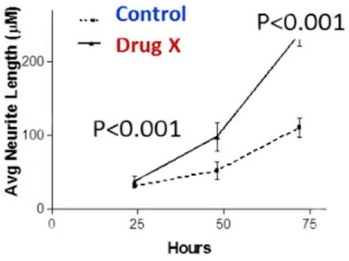


- Neurite Outgrowth Assay in PCN and PHN

Neurite outgrowth is an important morphological phenotype of neuronal cells. As the cellular processes are essential for cell health and function, test compounds that can affect the growth of neurites may have potential as drugs for neuropathological disorders. In this assay, effects of test compounds on neurite outgrowth are tested with fluorescent staining.

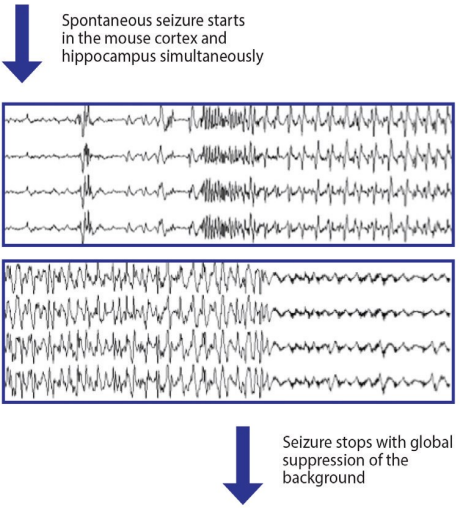




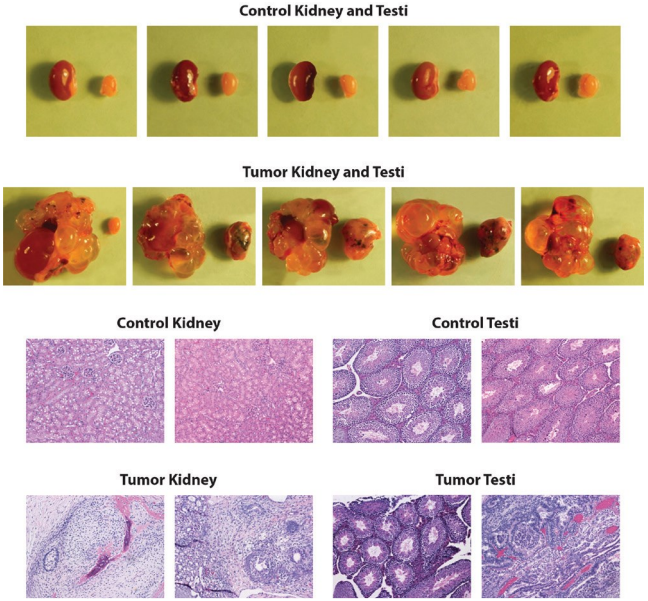


Neurophysiology
(Dr. Brenda Porter)

- Continuous EEG to assess rodents for seizure activity



Non-GLP Safety and Pathological Evaluation



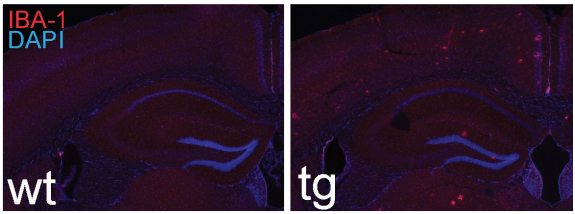
Biochemical and Histochemical Evaluation

- General histological stains
- Immunohistochemistry using the ABC/DAB method
- Immunofluorescence for various cellular markers
- Biochemical evaluation of samples

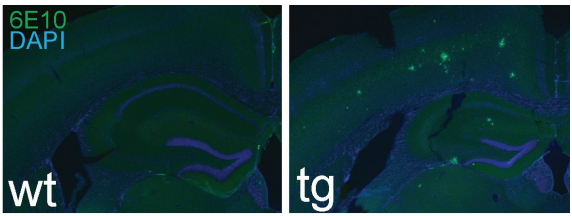
Neuropathological assessment in models of Alzheimer's Disease

- Immunohistochemistry

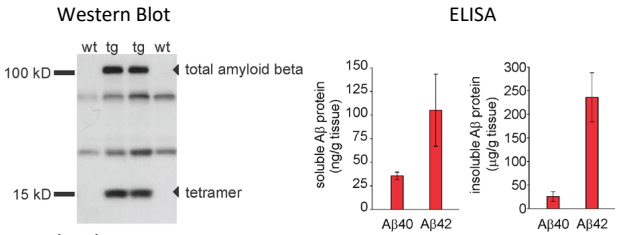
Microglia Staining (IBA-1-immunoreactivity)



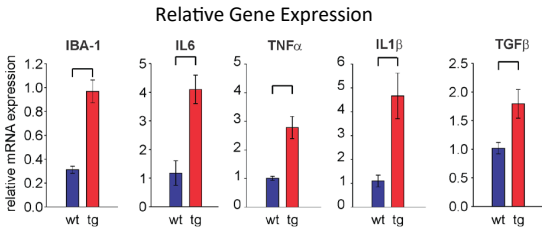
Amyloid Beta Plaque Staining (6E10-immunoreactivity)



- Amyloid Beta Plaque Load



- Quantitative rtPCR



Price Chart FY2019

Service	FY19 Rate/Hour
Experiment performed by BFNL Staff	$ 127
Facility/BFNL Equipment Use	$ 66
Technical Procedure Room Use	$ 32
Ph.D. Level Data Interpretation	$ 127

Service	Description	FY19 Estimated Rate/Animal*
Fear Conditioning	Three day learning and memory assay	$76
Y-Maze	Spontaneous alternation test of working memory	$25
Morris Water Maze	Seven day spatial memory test	$177
Catwalk	Motor function and coordination assay	$50
Open Field	General and locomotor activity assay	$34
Elevated + Maze	Anxiety-related behavior assessment	$26
Pre-Pulse Inhibition	Four day startle response assay	$126
Passive Avoidance	Learning and memory assay	$76
Rota-Rod Test	Motor coordination and balance assay	$37
Automated home cage testing	Long-term home cage observations of activity (max 24 mice)	$286
Light/Dark box	Anxiety and activity assay	$34

* Price per mouse for data acquisition

Contact Us

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