inotiv
analyze. answer. advance.

Advanced Parkinson's Disease Research

Validated and Established Disease Models and Assays

Utilize Inotiv's portfolio of products and services for discovery and preclinical drug development. We offer validated and established transgenic and non-transgenic disease models, as well as *in vivo* and *in vitro* assays, that are developed to deliver translationally relevant data that can drive the development of therapies for Parkinson's disease (PD).

Animal Models of PD

Inotiv is the preferred source of animal models for PD. We offer both transgenic rat models, originally created at SAGE Lab, Inc., that express genetic mutations associated with PD, and commonly used chemically induced models that mimic the loss of dopamine neurons seen in this disease. Additionally, we are proud to offer select models sponsored by The Michael J. Fox Foundation for Parkinson's Research (denoted by *). These models do not require a breeding license or MTA for purchase.

Genetically Engineered Models

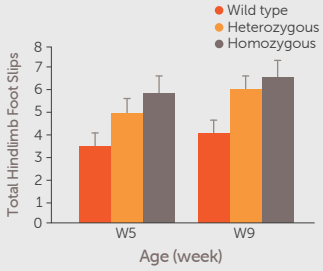
- AAV-A53T α-synuclein mouse/rat
- α-Synuclein A53T knockin rat*
- α-Synuclein knockout rat*
- Lrrk1 knockout rat
- Lrrk2 knockout rat
- Lrrk1-Lrrk2 knockout rat
- Park2 (Parkin) knockout rat
- Park7 (DJ-1) knockout rat
- Pink1 (Park6) knockout rat
- Pink1/Parkin knockout rat*

Chemically Induced Models

- 6-hydroxydopamine (6-OHDA)-induced rats
- 6-OHDA-induced mice

Figure 1 Hindlimb Foot Slips by Pink1 (Park6) Knockout Rats

Pink1 (Park6) heterozygous (orange bars) and homozygous (grey bars) knockout rats displayed increased hindlimb foot slips on a tapered balance beam compared to wild type animals (red bars) at both 5 and 9 weeks of age. There were no differences in forelimb foot slips between the groups (data not shown).



Behavioral Assays

Inotiv offers a large selection of behavioral tests to assess movement impairments in PD animal models. Our assays are indispensable tools for evaluating the magnitude of dopamine neuron loss as well as the effectiveness of neuroprotective therapies meant to maintain or restore functioning of the nigrostriatal dopamine pathway.

- Cylinder test
- Rotarod test
- Light/dark box test
- Open field assay
- Gait analysis
- Apomorphine-induced rotation behavior
- Amphetamine-induced rotation behavior
- Elevated plus maze
- Swim test
- Barnes maze
- Morris water maze
- Contextual fear conditioning

Figure 2 Amphetamine Induces Ipsilateral Rotation in 6-OHDA Rats

Rats with unilateral 6-OHDA induced damage of the nigrostriatal dopamine pathway (6-OHDA, n=22; orange line) displayed an increased rotation rate toward the side of the lesion compared to control animals (SHAM, n=11; red line).

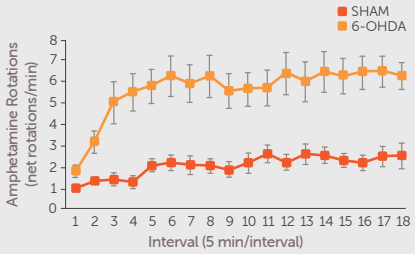
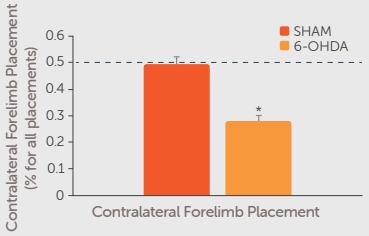


Figure 3 Asymmetrical Forelimb Use by Unilateral Dopamine-Depleted Rats

Rats with unilateral 6-OHDA induced damage of the nigrostriatal dopamine pathway (6-OHDA, n=22) and control animals (SHAM, n=11) were tested for locomotor asymmetry using the cylinder test. 6-OHDA rats showed a significant decrease in the percentage of contralateral forelimb contacts (orange bar) compared to control animals (red bar).



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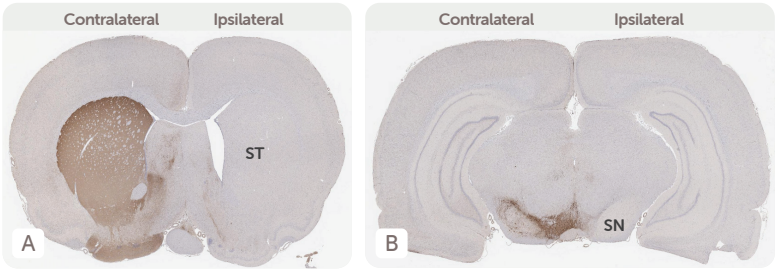
Histopathological Assessment

Inotiv offers advanced capabilities for histopathological assessment of neural tissue from PD animal models. Utilize our experts to design your custom assay to characterize 6-OHDA lesions, assess neurochemical expression, evaluate glial cell reactivity, or answer other questions that can accelerate your PD research program.

Figure 4 Ipsilateral Depletion of Dopaminergic Neurons Following Unilateral MFB Lesioning

Expression of tyrosine hydroxylase (TH), the rate limiting enzyme in dopamine synthesis, was detected in perfusion fixed, paraffin embedded sections of brain from a rat that received a unilateral injection of 6-OHDA into the medial forebrain bundle (MFB). TH-positive neurons were detected in the striatum (**A;** ST) and the substantia nigra (**B;** SN) on the contralateral side of the 6-OHDA-induced lesion while TH immunoreactivity was absent in both nuclei on the ipsilateral side.

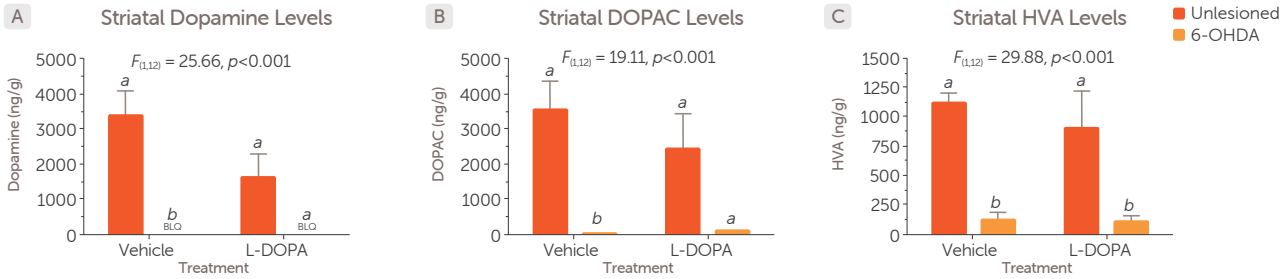


Additional Services for PD Research

Inotiv's capabilities extend beyond models and behavioral testing. Other services include GLP and non-GLP *in vivo* and *in vitro* assays that can be customized to provide solutions for your PD research program.

- Stereotaxic surgery
- Tissue harvesting
- Oxidative stress enzymology
- Neurotransmitter and metabolite quantification
- CBC/clinical chemistry analysis
- Mass spectrometry proteomics
- Primary neural cell culturing
- Human stem cell and brain organoid culturing
- Confocal & electron microscopy

Figure 5 Ipsilateral Depletion of Dopamine Levels Following Unilateral MFB Lesioning



The levels of dopamine **(A)** and dopamine metabolites, DOPAC **(B)** and HVA **(C)**, in the striatum of rats that received a unilateral injection of 6-OHDA into the MFB were measured 60 minutes after being treated with either L-DOPA or vehicle. Dopamine, DOPAC, and HVA were detected in the striatum on the contralateral side of the 6-OHDA-induced lesion (red bars) but were depleted in the ipsilateral nuclei (orange bars).

Contact us at inotivco.com/contact to discuss how our models and services can support your PD research.