



PRECLINICAL RESEARCH

- Neurology and Psychiatry
Drug Profiling
- *In Vivo* and *In Vitro* Assays
- Behavioural Tests
- Nerve fiber morphometry
- Nerve conduction studies

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NEUROFIT

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NEUROFIT offers comprehensive list of disease models in rodents for assessing the efficiency of drug candidates. Studies include quantitative behavioural measurements to evaluate the impact of the treatment on the disease symptoms.

1. ■ NEUROLOGY PROGRAM

Diseases	Therapeutic screening target	Models
Alzheimer's disease	■ procognitive drugs	<ul style="list-style-type: none"> ■ Scopolamine-induced cognitive deficit ■ Methyllycaconitine-induced cognitive deficit ■ Cognitive deficit in aged mouse
	■ disease modifier drugs	<ul style="list-style-type: none"> ■ icv Aβ - induced cognitive deficit
Schizophrenia	■ procognitive drugs	■ MK-801-induced cognitive deficit
		■ Phencyclidine-induced cognitive deficit
Parkinson's disease	■ disease modifier / symptomatic drugs	■ 6-OHDA –induced hemiparkinson lesion
	■ Anti-akinesia effect	■ Haldol-induced akinesia
Epilepsy	■ Anticonvulsive drugs	■ PTZ-induced convulsion
Peripheral neuropathies	■ Neuroprotectant, neuroregenerative drugs (Nerve repair / regeneration)	<ul style="list-style-type: none"> ■ Sciatic nerve crush ■ Diabetes-induced neuropathy (STZ-rats)
Neuropathic pain	■ Pain relief drugs	■ Diabetes-induced neuropathic pain (STZ rats)
		■ Formalin test
		■ Acute pain

NEUROFIT offers a variety of well-accepted behavioural tests to assess the potential anxiolytic, antidepressant, antipsychotic or procognitive effect of test compounds. In addition, animal models have been established in order to better mimic the clinical symptoms of these disorders. Assays and models are validated with drugs used in clinic setting (reference compounds).

2. ■ PSYCHIATRIC & COGNITIVE DISORDERS

TEST	ANIMAL MODELS
■ ANXIETY <ul style="list-style-type: none"> ■ Light-dark test ■ Marble burying ■ Elevated plus maze 	<ul style="list-style-type: none"> ■ CCK-4 –induced panic anxiety ■ Yohimbine-induced panic anxiety
■ DEPRESSION <ul style="list-style-type: none"> ■ Tail suspension test ■ Forced swimming test 	
■ SCHIZOPHRENIA <ul style="list-style-type: none"> ■ hyperactivity in open-field 	<ul style="list-style-type: none"> ■ MK801-induced hyperactivity ■ D-amphetamine-induced hyperactivity ■ Phencyclidine-induced hyperactivity
■ CATALEPSY	<ul style="list-style-type: none"> ■ Haldol-induced catalepsy
■ COGNITIVE & MEMORY DEFICIT <ul style="list-style-type: none"> ■ Object recognition test ■ T-maze ■ Y-maze ■ Passive avoidance test 	<ul style="list-style-type: none"> ■ Scopolamine-induced cognitive deficit ■ MK-801-induced cognitive deficit ■ Phencyclidine-induced cognitive deficit ■ Methyllycaconitine-induced cognitive deficit ■ Natural forgetting
■ ATTENTION DEFICIT HYPERACTIVITY DISORDERS <ul style="list-style-type: none"> ■ T-maze 	<ul style="list-style-type: none"> ■ Scopolamine-induced attention deficit
■ SIDE EFFECTS <ul style="list-style-type: none"> ■ Open field ■ Rotarod test ■ Memory tests ■ String test 	

NEUROFIT provides *in-vivo* models for inflammatory, contact allergic and autoimmune diseases.

3. INFLAMMATION PROGRAM

Diseases	Therapeutic screening target	Models
Multiple sclerosis	Disease modifiers / neuroprotectant	<ul style="list-style-type: none"> ■ Relapsing-Remitting EAE in Dark-Agouti rats ■ MBP-EAE in Lewis rats
Rheumatoid arthritis	Immunomodulators, anti-inflammatory, immuno-suppressors	<ul style="list-style-type: none"> ■ Pristane-induced Rheumatoid arthritis ■ Collagen-induced Rheumatoid arthritis
Allergic contact dermatitis	Immunomodulators, immuno-suppressors, anti-inflammatory drugs	<ul style="list-style-type: none"> ■ Oxazolone-induced allergic contact ■ Ovalbumin-induced allergic contact
Acute inflammation	Immunomodulators, immuno-suppressors, anti-inflammatory drugs	<ul style="list-style-type: none"> ■ Carrageenan mouse air pouch model

NEUROFIT offers a comprehensive neurocellular models and assays for evaluating neurotoxicity, neuroprotection or neurotrophic activity of new test compounds.

NEUROFIT can also develop custom protocols to determine mechanism of action, or define therapeutic indication of new drug candidates.

4. ■ NEUROCELLULAR MODELS

RAT PRIMARY CULTURES	<ul style="list-style-type: none"> ■ Cortical, Hippocampal, Mesencephalon neurons ■ Spinal cord motoneurons ■ Sensory neurons ■ Schwann cells – sensory neurons co-culture ■ Rat nerve - human muscle co-culture ■ Glial cells: astrocyte or oligodendrocyte precursor
MODELS	<ul style="list-style-type: none"> ■ Parkinson's models: survival of mesencephalic dopaminergic neurons intoxicated with MPP+ or with 6-OHDA ■ Alzheimer's model: survival of hippocampal neurons intoxicated by Aβ1-40 ■ ALS model (Excitotoxicity): survival of neurons intoxicated with glutamate or NMDA ■ Co-culture nerve/muscle: effects of test compounds on co-culture innervation ■ Multiple sclerosis: Oligodendrocyte precursor proliferation ■ Stroke: survival of neurons intoxicated with glutamate or NMDA ■ Peripheral neuropathies: survival of DRG neurons intoxicated with cisplatin, vincristine or taxol; survival of spinal motor neurons intoxicated with vincristine
ASSAYS	<ul style="list-style-type: none"> ■ Viability and survival tests: LDH, AP, MTT assays ■ Neurotrophic effect: neurite length and density, number of branch point neuritis ■ Western blotting of proteins ■ Co-culture: length of neurites, surface of innervated muscle fiber area, innervation rate, video samples

5. NERVE FIBER MORPHOMETRY ANALYSIS

NEURODEGENERATION INVESTIGATION ON PERIPHERAL NERVES

(computer-assisted analysis of nerve fiber morphometry)

- Axon size distribution, axon density
- g-ratio distribution (Myelin thickness)
- Debris clearance
- Regenerating axons
- Nerve caliber

6. NERVE CONDUCTION STUDY

NEUROFIT performs nerve conduction study in various animal models of nerve injury, peripheral neuropathy and myopathy in order to evaluate the impact of drug treatment on nerve-muscle function.

Nerve conduction studies consist of:

- **compound muscle action potential (CMAP)**
also known as motor nerve conduction study
- **sensory nerve action potential (SNAP)**
also known as sensory nerve conduction study