

# KNOWLEDGE ISENTHING

Like the brain, neuroscience has a multitude of layers. Our broad solutions, innovative technologies, and proven expertise help researchers like you understand neurological diseases so that patients can benefit from better treatments and therapies.

Neuroscience investigates the complexity of structure and function behind the brain and the neurological processes of the nervous system, relying on scientific expertise across a diverse spectrum of techniques, from molecular biology to psychology.

Neurological disorders encompasses large umbrellas of neurodevelopment diseases, psychiatric disorders, and neurodegenerative diseases, which are characterized by cell death and/or loss of function in certain parts of the brain and nerve cells that stop normal organ function. Neurological disorders also include neuromuscular, neuroimmune, and neuro-ophthalmology diseases, among others.

As the world population steadily ages, neurodegenerative diseases such as Alzheimer's and Parkinson's continue to affect millions of people globally. It's critical to better understand the fundamental processes and microsystems of the neurons and circuits underlying these complex neurodegenerative diseases so that we can improve patient outcomes.

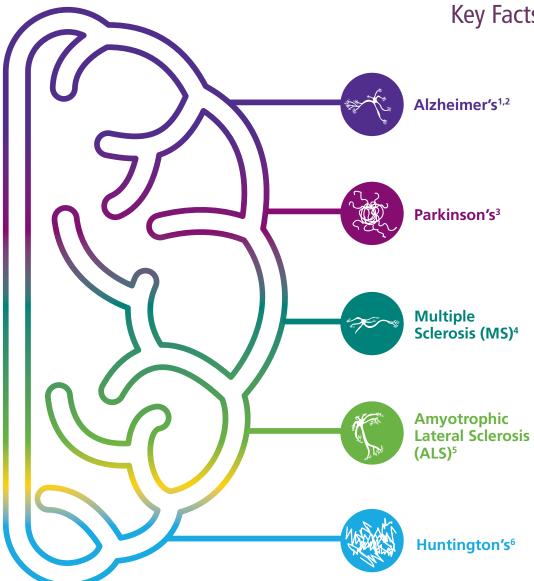
Researchers are using technologies at the forefront of cellular and molecular biology, imaging, and analytics to help elucidate disease development and aid in clinical research for potential therapies for neurological disorders. Our unwavering goal is to help you continue that exploration with a product portfolio that delivers reliable reagents, instruments, and services, accelerating molecular and therapeutic discoveries.

Neuroscience and Neurodegenerative Disease Overview



### **5 NEUROLOGICAL DISEASES**

Key Facts and Figures



- Characterized by atrophy of the cerebral cortex, and certain sub-cortical regions
- Affects 50 million people worldwide
- Women are more at risk than men
- Long-term degenerative disorder with motor symptoms caused by dopaminergic neuronal death in the midbrain region
- Affects 7 million to 10 million people worldwide
- Men are more at risk than women
- Brought about by irreversible axonal loss caused by the immune system's attack on myelin sheaths that protect nerve fibers
- The most common disabling neurological condition in young adults
- Women are two to three times more affected than men
- Characterized by loss of voluntary muscle control due to neuron death
- Part of the motor neuron disease (MND) group
- Also known as Lou Gehrig's disease
- A rare, inherited disease caused by a single-gene defect that leads to progressive decline in movement, cognition, and mental/physical capability
- Symptoms often appear in patients in their 30s or 40s
- An autosomal dominant transmission with one defective copy

- 1. www.alz.org/alzheimers-dementia/facts-figures
- 2. www.cdc.gov/aging/aginginfo/alzheimers.htm
- 3. www.parkinson.org
- 4. www.healthline.com/health/multiple-sclerosis/facts-statistics-infographic#5
- 5. www.als.org
- 6. hdsa.org

Neuroscience and Neurodegenerative Disease Overview





# Alzheimer's

**Disease** 



#### Did you know...

More than



#### **MILLION**

Americans have been diagnosed with Alzheimer's disease (AD)

The disease kills more people than breast cancer and prostate cancer combined



LEADING cause of death in the United States

# 

dies from AD or another dementia

Symptoms can first appear after age 60, and the risk increases with age



Young people may develop AD, but it is less common

The number of people over age 65 with Alzheimer's doubles every five years, and that number is expected to reach

14 million by 2060





+ 65 years

https://www.alz.org/alzheimers-dementia/facts-figures https://www.cdc.gov/aging/aginginfo/alzheimers.htm





5 Key Facts About

# Parkinson's

Disease



#### Did you know...



#### 1 MILLION PEOPLE

in the U.S. will be living with Parkinson's disease (PD) by 2020 – more than the combined number of people living with multiple sclerosis, muscular dystrophy, and amyotrophic lateral sclerosis (ALS)



APPROXIMATELY 60,000

Americans are diagnosed

with PD each year

More than
10 MILLION
people worldwide
are living with PD



Incidence of PD increases with age, but an estimated 4% of people with PD are diagnosed before age 50



www.apdaparkinson.org





# Multiple Sclerosis (MS)

Disease



**MORE WOMEN HAVE MS** The disease is 2 to 3 times more common in women than men



In southern U.S. states. the rate of MS is between 57 and 78 cases per 100,000 people. The rate is twice as high in northern states at about 110 to 140 cases per 100,000

**15%** of patients have one or more family members or relatives who

also have MS

**MULTIPLE SCLEROSIS** is NOT considered an inherited disorder, but researchers believe there may be a genetic predisposition to developing the disease

Multiple sclerosis is the most widespread disabling neurological condition of young adults between the ages of 20 and 50

Since the exact cause of MS is still unknown, there's no known prevention or cure, but treatments can help manage symptoms

www.healthline.com/health/multiple-sclerosis/facts-statistics-infographic#Prevalence



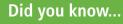




6 Key Facts About

# **Amyotrophic Lateral** Sclerosis (ALS)

Disease



90% of ALS cases are sporadic

ALS can affect all races or ethnic backgrounds, at any age

5,000 PEOPLE in the U.S. are diagnosed with ALS each year



more people die every year from ALS than Huntington's disease or multiple sclerosis

It is estimated that as many as 30,000 Americans are living with amyotrophic lateral sclerosis

The life expectancy of an ALS patient averages 2 to 5 years from the time of diagnosis -20% live longer than 5 years

**APPROXIMATELY** 









http://www.alsfoundation.org/learn/facts.htm





Neuroscience and Neurodegenerative Disease Overview



# Huntington's

Disease



Did you know...

# HUNTINGTON'S DISEASE (HD)

causes the progressive breakdown of nerve cells in the brain



Today, there are about 41,000 Americans living with HD and more than 200,000 who are at-risk of inheriting the disease



# **SYMPTOMS**

usually appear between the ages of 30 to 50 and worsen over 10 to 25 years



THE SYMPTOMS OF HD are described as having ALS, Parkinson's, and Alzheimer's simultaneously



Every child of a parent with HD has a 50/50 chance of inheriting the faulty gene The average length of survival after diagnosis is typically 10 to 20 years, but some people have lived 30 or 40 years



https://hdsa.org/#



# PROTEIN AGGREGATION

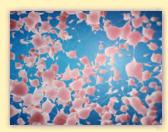
Through extensive research, scientists have discovered that excess or unnatural protein aggregations have been implicated in many neurodegenerative disorders – and their progressions – due to the toxicity of tangles and fibrils in the neurons and within the ecosystem of a properly functioning nervous system.

The progression and symptoms of Alzheimer's, Parkinson's, Huntington's, and several others have been linked to aggressively expanding aggregates such as tau,  $\beta$ -amyloids,  $\alpha$ -synucleins, and mutated huntingtin.

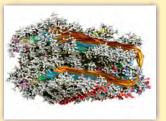
Understanding the biological processes involved in the regulation, formation, dysregulation, and potential remedies for protein aggregation is crucial to treating these diseases.

Labs everywhere are exploring the roles of molecules and biological steps associated with misfolding, mutations, excess seeding, oligomerization, phosphorylation, and clearance of these proteins and polypeptides, while several pharmaceutical and biotech leaders are developing neutralizing antibodies and exploring other therapeutic avenues like proteolysis targeting chimera (**PROTACs**).

Different methodologies exist for assaying protein aggregates, and they range in sensitivity and throughput. We have the expertise to support your technology and platform of choice for protein aggregate detection for disease staging studies or biomarker determination in cerebrospinal fluid (CSF).



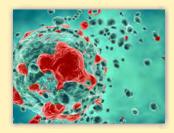
Read an application note about tau protein aggregation assay relevant to Alzheimer's disease and tauopathies research.



View our poster to learn about secreted APP and amyloid beta quantification in SH-SY5Y cell media.



Learn more about the detection of total, phosphor, and aggregated α-synucleins in biological samples.



Read more about innovative therapeutic strategies against Huntington's disease.



Read a publication highlight about how infection with mosquito-borne alphavirus induces selective loss of dopaminergic neurons, neuroinflammation, and widespread protein aggregation

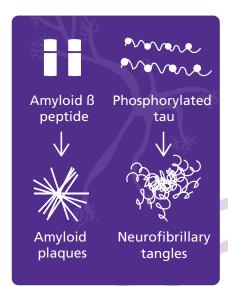
**Protein Aggregation** 



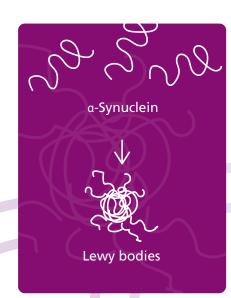
## **NEUROLOGICAL DISEASES**

and Associated Protein Aggregates

**Alzheimer's Disease** 



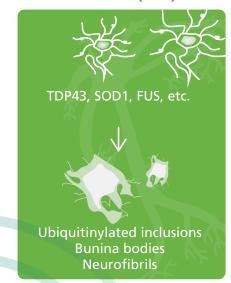
**Parkinson's Disease** 



**Huntington's Disease** 



Amyotrophic Lateral Sclerosis (ALS)



**Protein Aggregation** 

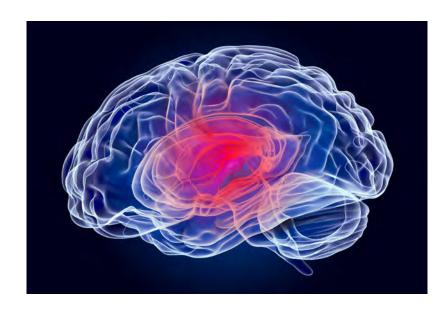


# **NEUROINFLAMMATION**

Following various stress cues, the central nervous system (CNS) activates its immune system to elicit a protective neuroinflammatory response. But if neuroinflammation becomes a chronic state, it can cause more harm to the body than good.

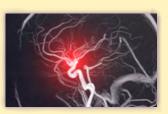
Microglial cells, astrocytes, and a variety of other cells collectively maintain homeostasis, safeguard neuronal synapse and bloodbrain barrier (BBB) integrity, help clear debris, and protect against neurotoxicity. However, their regulation of the neuroinflammatory response via NF- $\kappa\beta$  activation and release of proinflammatory cytokines such as TNF- $\alpha$ , IL-1 $\beta$ , and IL-6 can become skewed if the anti- and pro-inflammatory balance is broken. This creates a neurotoxic environment.

Researchers continue to explore the pathological conditions that lead to neurotoxicity and decrease in neuroprotective agents, which also links to excess and chronic neuroinflammation in various *in vitro* and *in vivo* models.





Read more about how scientists are leveraging immunoassays to move multiple sclerosis drug discovery forward.



Read our whitepaper to learn about vaccine research and the impacts of COVID-19 on neurological systems.



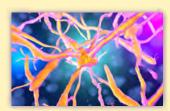
Read an application note to learn more about neuroinflammation on TREM2 and Syk signaling in human IPSC-derived macrophages using HTRF.



Join an on-demand webinar to learn more about linking neuroinflammation and neurodegeneration.



Attend our webinar to learn more about in vivo molecular imaging applications in gene editing and neuroinflammation.

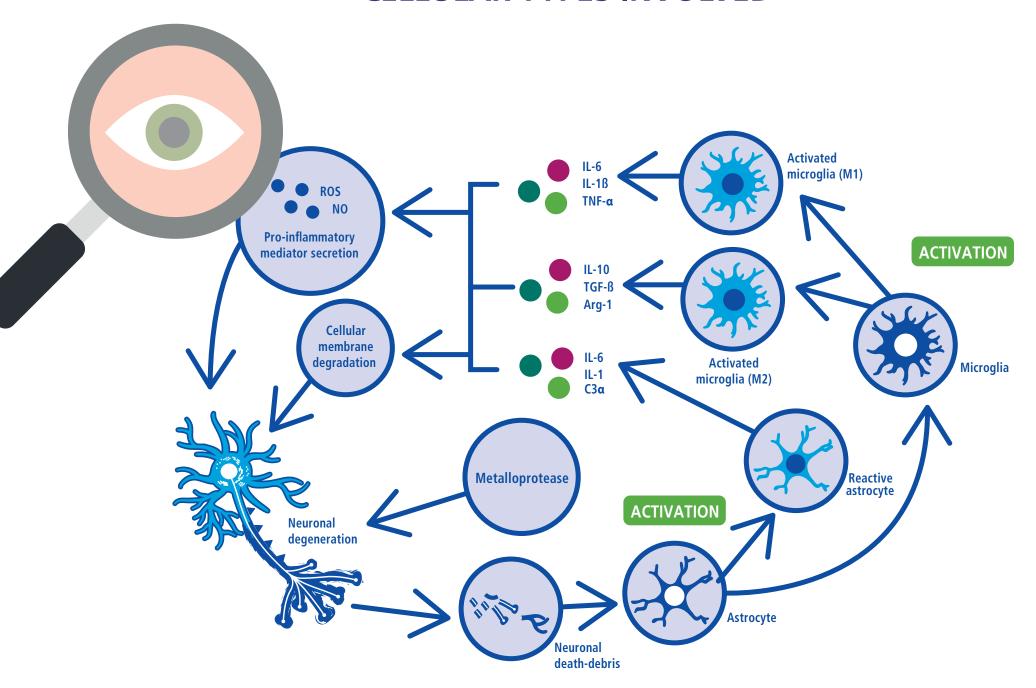


Read an application note for more information about neuroinflammation research solutions using HTRF assays.

Neuroinflammation



# **CELLULAR TYPES INVOLVED**



Neuroinflammation



# ALTERED CELLULAR PROCESS

In addition to abnormal protein dynamics, other biologically important cellular processes that are critical to proper brain and nerve function can be affected by neurodegenerative diseases. These processes include simple or complex multiregulated pathways and broad processes.

- Disruptions in cell apoptosis
- Necrosis
- Cell cycle regulation or arrest
- Autophagy
- Proteostasis
- Lysosome disfunction or lipid peroxidation
- Bioenergetics or mitochondrial disfunction
- Oxidative or ROS stress
- Critical protein-protein or GPCR interactions
- Intercellular communication or kinase/phosphatase function

Along with these mechanistic process alterations, labs also look to specific **epigenetic** modifications, especially when age and environmental exposures and trauma impact neuroprotection and neurodegeneration.

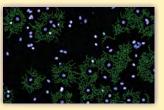
We offer researchers the tools and expertise to explore all the cellular processes involved in maintaining healthy neuronal and brain function and apply it to potential therapeutic targets. From proven instruments to reliable consumables to reagents such as HTRF, ALPHA, radiochemicals, and NGS library prep kits, researchers are empowered to successfully execute complex *in vitro* assays, high-content screening, and *in vivo* preclinical imaging applications.



Learn more about the pathways involved in neuroinflammation and neurodegeneration.



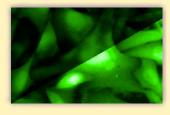
Read a blog post about potential neuroprotection of A2AR antagonists via modulation of NMDAR activity.



Read our case study about highcontent analysis of drug-induced oligodendrocyte differentiation promoting remyelination in multiple sclerosis.



Check out our whitepaper on using radioligands for neurochemical research.



Learn more about our fast kinetic calcium flux high content screening assay.



View our brochure about 3D multimodality imaging for disease research.

**Altered Cellular Processes** 



# RARE DISEASES

Alzheimer's, Parkinson's, and other prevalent neurological diseases are typically associated with neurodegeneration. They're multifactorial with complex genetic and environmental associations and a spectrum of symptoms and severities. However, rare diseases also exist within neurological disorders. And thanks to contributions and awareness from advocacy groups and federal incentives, some of these diseases are actively researched for the eventual development of orphan drugs for ALS, Huntington's, Friedreich's ataxia, and spinal muscular atrophy (SMA).

Early research of these rare diseases revolved around understanding the genetic causes. Huntington's, Friedreich's ataxia, and SMA are among those that are caused by mutations to a single gene and typically follow canonical recessive or dominant inheritance patterns and associated risks. Others, like ALS have several genetic mutations associated and are found to be more sporadic in nature.

For many years, academic, biotech, and pharmaceutical researchers have collaborated to expand the understanding of these rare diseases through basic and translational research, for the eventual development of novel methods for the accurate detection of mutations or other genetic contributors. As a result, they've developed proven platforms integrating modification technologies like <a href="CRISPR/Cas9">CRISPR/Cas9</a> and <a href="AAV delivery methods">AAV delivery methods</a>, offering promising new therapies.



Read our publication highlight to learn more about age-dependent SMN expression in disease-related tissue post-mortem from ASO-treated, nontreated, agematched, and control patients.



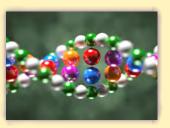
Learn more about engineered human neural stem cells (NSCs) expressing varying Exon 1 HTT fragments are used to study Huntington's disease.



Check out our poster about comprehensive clinical testing for spinal muscular atrophy.



Join our webinar on preimplantation genetic testing for monogenic (PGT-M) disorders.



Read about NFFinder, a free web-based bioinformatic research tool for neurofibromatosis (NF) and rare disease.

**Rare Diseases** 



### BIOMARKER AND DRUG DISCOVERY

In neurodegenerative disorders, proper and early diagnoses can help slow the disease progression and severity of symptoms. Researchers continue to search for accurate biomarkers for disease staging and identify at-risk patients using rapid, high-throughput methods for genetic and molecular markers – all by using biological samples that are less invasive than brain imaging or biopsy.

Coupled with biomarker discoveries, therapies and drug developments are necessary to tackle neurological disorders for disease and symptom management. Small-molecule therapeutics and biologics have faced unique hurdles simply because the CNS and PNS are so multifaceted and complex. As a result, there have been minimal strides made in the last few decades. Barriers to consider include the following:

- Creative delivery methods
- Bioavailability to the brain and nervous system
- Aspects of neuroimmunomodulation
- Severity of side effects
- Influence of the gut microbiome
- Stringency of the blood brain barrier (BBB)

Although there is currently no cure, researchers are unyielding. To help stack the odds for a likely therapeutic response, investigators are working diligently and making significant progress as more genetic and molecular pathways are mapped out.

Recently, a branch of research has leveraged the principles of regenerative medicine by exploring stem cells for cell replacement or niche enrichment by the addition and production of neuroprotective factors.

The study of the efficacy and safety of innovative drugs can be accelerated through technologies like HTS automation and multimode plate readers, HCA, and preclinical *in vivo* imaging along with reliable QC/QA tools.



Read our case study on improving the throughput of a neuroprotection assay using the Opera Phenix high-content screening system.



View our application note to learn more about the role of *in vivo* imaging in drug discovery and development.



Join a genome webinar about small RNA profiling for drug discovery and CDx.



Learn more about reversing the damages of Multiple Sclerosis.



Read our application note about stem cells for preclinical imaging.



View our application note about the culture and QC of human iPSCderived neuronal cells using an automated HT approach and multimode detection system.



Read our white paper on biomarker profiling, focusing on small RNAs.

Biomarker and Drug Discovery



## **GENOMICS**: Automation Improves Workflow Efficiency

Genomic insights can help provide better understanding into neurological processes and disease states, especially in rare disease research of genetic origin, microbiome profiling, and biomarker discovery. Some potential therapeutics also relies on exploring genetic, transcriptomic, and epigenetic information surrounding nervous system disorders.



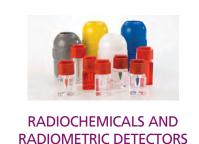






## **DETECTION**: Innovative, Integrated Solutions That Accelerate Your Workflow

Molecular assays that are robust, sensitive, easy-to-use, and high-throughput help neuroscience researchers identify faulty cellular pathways and explore disease- or symptom-causing culprits such as peptide aggregates, neuroinflammation, overactive proteins or enzymes, inappropriate interactions, and altered post-translational modifications.







MICROPLATES



Research Technologies



## **CELLULAR IMAGING:** Phenotype Cellular Responses

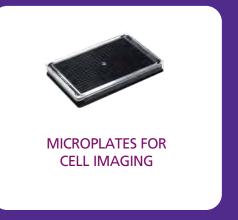
Researchers can rely on robust cell-based imaging instruments, consumables, reagents, and analytics to decipher molecular and cellular processes critical to understanding neurological pathogenesis and disease progression.





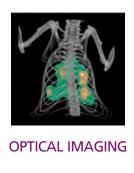






## IN VIVO IMAGING: The Power of Preclinical Imaging

Preclinical information captured via small animal in vivo imaging can help elucidate systemic- and organ-level effects that can help provide a more comprehensive view of neurological disorders and the complexity involved in drug discovery and development, not limited to systemic or neuroinflammation, efficacy of delivery methods/therapies, bioavailability of compound or imaging module, stringency of BBB, potential off-target effects, and toxicology profiles.







**Research Technologies** 



For more information visit <u>www.perkinelmer.com/category/neuroscience-research</u>

PerkinElmer, Inc. 940 Winter Street Waltham, MA 02451 USA P: (800) 762-4000 or (+1) 203-925-4602 www.perkinelmer.com

