LifeLabs Genetics offer a variety of single gene tests and next generation sequencing panels for a variety of inherited neurological conditions:

Conditions	Selected Neurology Panels
Epilepsy	• Absence epilepsy in childhood • Dravet syndrome • Epileptic encephalopathy • Generalized epilepsy with febrile seizures • Hereditary partial epilepsy • Hyperekplexia
Dementia	• Alzheimer disease • Frontotemporal dementia
Motor Neuron Disease	• Amyotrophic lateral sclerosis (ALS) • Spastic paraplegia
Movement Disorders	• Dystonia • Cerebellar ataxia • Episodic ataxia • Familial hemiplegic migraine • Parkinson disease • Spinocerebellar ataxia
Peripheral Neuropathy	• Charcot Marie Tooth disease • Dejerine-Sottas syndrome
Neuromuscular Disease	• Congenital myasthenic syndrome • Congenital myopathy • Limb-girdle muscular dystrophy • Malignant hyperthermia • Metabolic myopathies • Nemaline myopathy • Walker-Warburg syndrome
Brain Disease and Developmental Delay	• Aicardi-Goutieres syndrome • Holoprosencephaly • Joubert syndrome • Leukodystrophy & peroxisome biogenesis disorders • Lissencephaly • Microcephaly • Neuronal migration disorders • Tuberous sclerosis • Zellweger syndrome • X-linked mental retardation
Mitochondrial Disorders	• Leigh syndrome and mitochondrial encephalopathy • Mitochondrial dysfunctions

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BRAIN DISEASE AND DEVELOPMENTAL DELAY

There are over 1,000 genetic disorders that affect the development and function of the brain. This large group of diseases includes leukodystrophies, peroxisomal biogenesis disorders, tuberous sclerosis and various forms of intellectual impairment linked to the X chromosome. Many of these diseases are progressive and increasing knowledge of how they damage the nervous system has led to new treatments that are most effective when initiated before there are symptoms, or when symptoms are still mild. **An accurate and early genetic diagnosis is essential as specific therapies are increasingly being recognized.**

MITOCHONDRIAL DISEASE

Mitochondria provide the energy for cell functions and are critical for the normal growth and development of most tissues and organs. Inherited disorders of mitochondrial function can present at any age and may affect a single organ or multiple systems. Symptoms include poor growth, loss of coordination, weakness, visual problems, hearing loss, learning disability, liver disease, kidney disease, gastrointestinal disorders, respiratory problems, neurological problems and dementia. These disorders are also associated with a high occurrence of pregnancy loss.
Genetic Diagnosis is important to facilitate screening and early treatment for potential complications such as diabetes, cataracts, heart disease, and seizures.

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RESOURCES

ALS Canada: http://www.als.ca
Alzheimer Society of Canada: http://www.alzheimer.ca/
Canadian Association of Genetic Counsellors: www.cagc-accg.ca
Epilepsy Canada: http://www.epilepsy.ca/
Parkinson Society of Canada: www.parkinson.ca/
Muscular Dystrophy Canada: http://www.muscle.ca

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The Field Of Genetics Is Always Evolving And So Are We Please Visit Our Website For A Current Test List

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Neurological Disorders

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An estimated 3.6 million Canadians of all ages and ethnicities are affected by neurological conditions. This number is expected to increase significantly in the coming years due to ageing of the population and longer life expectancy. Many common conditions, such as epilepsy, Alzheimer disease and Parkinson disease, can be genetic. There are over 200 inherited neurological disorders that collectively affect almost 1% of the population.

WHAT YOU NEED TO KNOW

Genetic neurological disorders are inherited diseases of the nervous system that are caused by defects in one or more genes. These diseases affect the brain, spinal cord, nerves and muscles, and often require complex lifelong healthcare management. However, symptoms vary greatly and may be severe or mild, progressive or non-progressive, and treatable or untreatable.

Inherited neurological disorders affect all ages, and in many patients, there is no family history of the disease. LifeLabs Genetics offers single gene tests and next generation sequencing test panels for a wide range of neurological conditions including:

- Epilepsy
- Dementia
- Motor neuron disease
- Movement disorders
- Peripheral neuropathy
- Neuromuscular disease
- Brain disease and developmental delay
- Mitochondrial disease

200 Plus inherited neurological disorders that collectively affect almost 1% of the population.

EPILEPSY

Epilepsy is a common neurological condition, affecting about 1 in 160 Canadians of all ages and ethnicities. This large group of disorders causes recurring, unprovoked seizures due to disturbances with electrical signaling in the brain. Nearly 70 percent of people with epilepsy can have good control of their seizures using appropriate medications.

There are more than 20 known genetic epilepsy syndromes, including several devastating childhood disorders that can be difficult to treat. An accurate and early genetic diagnosis is essential for disease management as specific interventions may be indicated based on the gene mutation identified

Dravet syndrome

- A severe form of infantile epilepsy that can lead to developmental delays and sudden unexplained death
- More than 70% of cases are due to a genetic mutation in the SCN1A gene (most of these mutations are not inherited so there is no family history of epilepsy)
- Certain drugs are effective in seizure control while others are likely to increase seizures
- **A correct diagnosis at any age can improve management of seizures and quality of life**

Lennox-Gastaut syndrome (LGS)

- A severe disorder associated with significant mental and behavioural regression due to uncontrolled seizures in infancy and early childhood
- Accounts for 1-4% of of childhood epilepsies and has environmental and genetic causes
- **Several drugs have been specifically approved for the treatment of LGS**

GLUT1 deficiency syndrome

- Caused by mutations in the SLC2A1 gene
- Associated with frequent seizures usually beginning in infancy
- **A high-fat, low- carb diet has been shown to control seizures in some patients**

DEMENTIA

More than 15% of Canadians over 65 have dementia and up to 10% have disease onset before age 65. Alzheimer disease and frontotemporal degeneration (FTD) are two common dementia disorders that can have genetic causes.

Alzheimer disease

- Most common cause of dementia
- Most cases present after age 65 and are not strongly genetic
- Up to 5% of patients have disease onset before age 60-65 and a positive family history (EOFAD)
- A genetic mutation is identified in 40-80% of families with EOFAD and in a small number of patients with early-onset disease without a family history
- **A prompt genetic diagnosis is important so that patients and their families can plan for the future before dementia becomes severe**
- **Early genetic diagnosis also facilitates access to medications that may help alleviate symptoms and improve quality of life**

Frontotemporal degeneration

- Second most common cause of dementia in individuals under age 65
- 40% of cases are inherited
- Some genes and mutations are associated with severe disease, Parkinsonism and resting tremor, and responsiveness to certain drugs
- **Genetic diagnosis may eliminate the need for other potentially invasive diagnostic tests such as lumbar puncture for cerebrospinal fluid analysis**
- **Genetic test results may predict disease severity and age of onset, facilitate screening for potential complications, and in some cases, predict responsiveness to medications**

15% of Canadians over 65 have dementia

Up to 5% of patients have Alzheimer disease onset before age **60-65**

MOTOR NEURON DISEASE

Motor neuron diseases affect the nerves that control voluntary muscle activity, such as walking, speaking, breathing and swallowing. The cause of most of these progressive diseases is unknown. Inherited motor neuron disorders include hereditary spastic paraplegias (HSP), spinal muscular atrophies (SMA), and some forms of amyotrophic lateral sclerosis (ALS).

ALS (Lou Gehrig disease)

- Most common cause of neurological death in Canada
- Rapidly progressive with onset typically between age 40 and 60
- Nearly 1/3 of patients are misdiagnosed and may undergo unnecessary surgeries
- 10% of patients with ALS have a family history of ALS, FTD or Parkinson disease
- A genetic mutation is identified in 15% of all cases (60-70% of cases with a family history)
- The C9orf72 gene accounts for 40% of familial cases and 7% of cases without a family history
- Up to half of patients with C9orf72 mutations also develop dementia
- Another common gene, SOD1, is not usually associated with dementia
- A specific SOD1 mutation is associated with rapid disease progression while another SOD1 mutation is associated with survival of more than 10 years
- A rare familial juvenile ALS form has onset between 3 and 10 years of age
- **A genetic diagnosis prevents potential unnecessary surgery due to misdiagnosis**
- **Genetic testing may predict prognosis and determine those at risk for dementia**
- **Genetic testing identifies individuals who may be eligible for gene specific research and clinical trial participation**

MOVEMENT DISORDERS

Movement disorders are a group of conditions characterized by impaired or involuntary movements. Spinocerebellar ataxia, episodic ataxia, and familial hemiplegic migraine are three inherited movement disorders. Parkinson disease, dystonia, and cerebellar ataxia can also be genetic.

Parkinson disease (PD)

- Second most common neurodegenerative disease after Alzheimer disease
- Affects 1 to 2 per 1,000 people in Canada (1% of people over 55, 3% of people over 75)
- Associated with tremor, slowness, stiffness, impaired balance and muscle rigidity
- 20% of patients develop dementia
- Average age of onset is 60 (20% are diagnosed before age 50, 5-10% before age 40)
- Mutations account for 2-3% of all cases and 50-60% of early-onset cases
- More than 10 genes are known to cause PD
- PARK2-related PD is associated with early onset disease and an excellent response to levodopa. Autosomal recessive PARK2 mutations are the most common cause of early-onset familial PD
- LRRK2 mutations are associated with mid to late-onset slowly progressive disease and dementia is uncommon. Patients with LRRK2-linked PD also respond favourably to L-dopa. Autosomal dominant LRRK2 mutations are the most common monogenic cause of late-onset and sporadic PD
- **Genetic test results may predict disease severity, facilitate screening for dementia, and predict responsiveness to medications**

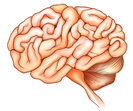
PERIPHERAL NEUROPATHY

Peripheral neuropathies are nerve disorders associated with numbness, tingling, weakness, and pain that typically starts in the feet and later affects the hands.

Charcot-Marie Tooth disease (CMT)

- Most common inherited peripheral neuropathy, affecting 1 in 2,500 people
- Diverse group of disorders associated with mutations in more than 80 genes
- Genetic mutation identified in 60-70% of cases (4 genes account for 90-95% of these)
- Disease onset is usually by age 20 although some mutation carriers never show signs
- 20-30% of patients have no family history
- **Genetic diagnosis may reduce the need for other invasive diagnostic tests such as EMG, nerve conduction, or nerve biopsy**
- **A number of drugs are toxic to CMT patients and should be avoided by both symptomatic and asymptomatic individuals with a genetic diagnosis**

3.6 million Canadians of all ages and ethnicities are affected by neurological conditions..



NEUROMUSCULAR DISEASE

Neuromuscular diseases affect the nerves that control skeletal muscles. Common symptoms include muscle weakness, rigidity, loss of coordination, twitching, spasms, and pain. Genetic neuromuscular diseases are individually rare, but together are estimated to affect 1 in 3,000 individuals. They may present at any age and include numerous muscular dystrophies, myopathies and malignant hyperthermia. There are more than 50 known genetic causes of muscular dystrophy alone.

Limb-girdle muscular dystrophy

- Characterized by hip and shoulder weakness
- More than 35 different genetic forms that affect all ages
- Mutations in 9 genes account for more than 95% of cases
- Some forms include cardiac and respiratory weakness while other forms are limited to skeletal muscle involvement
- **A precise genetic diagnosis is important to determine which patients require close monitoring and/or early intervention for potential pulmonary and heart complications**