NEW GENETIC TESTING FOR PARKINSON'S DISEASE

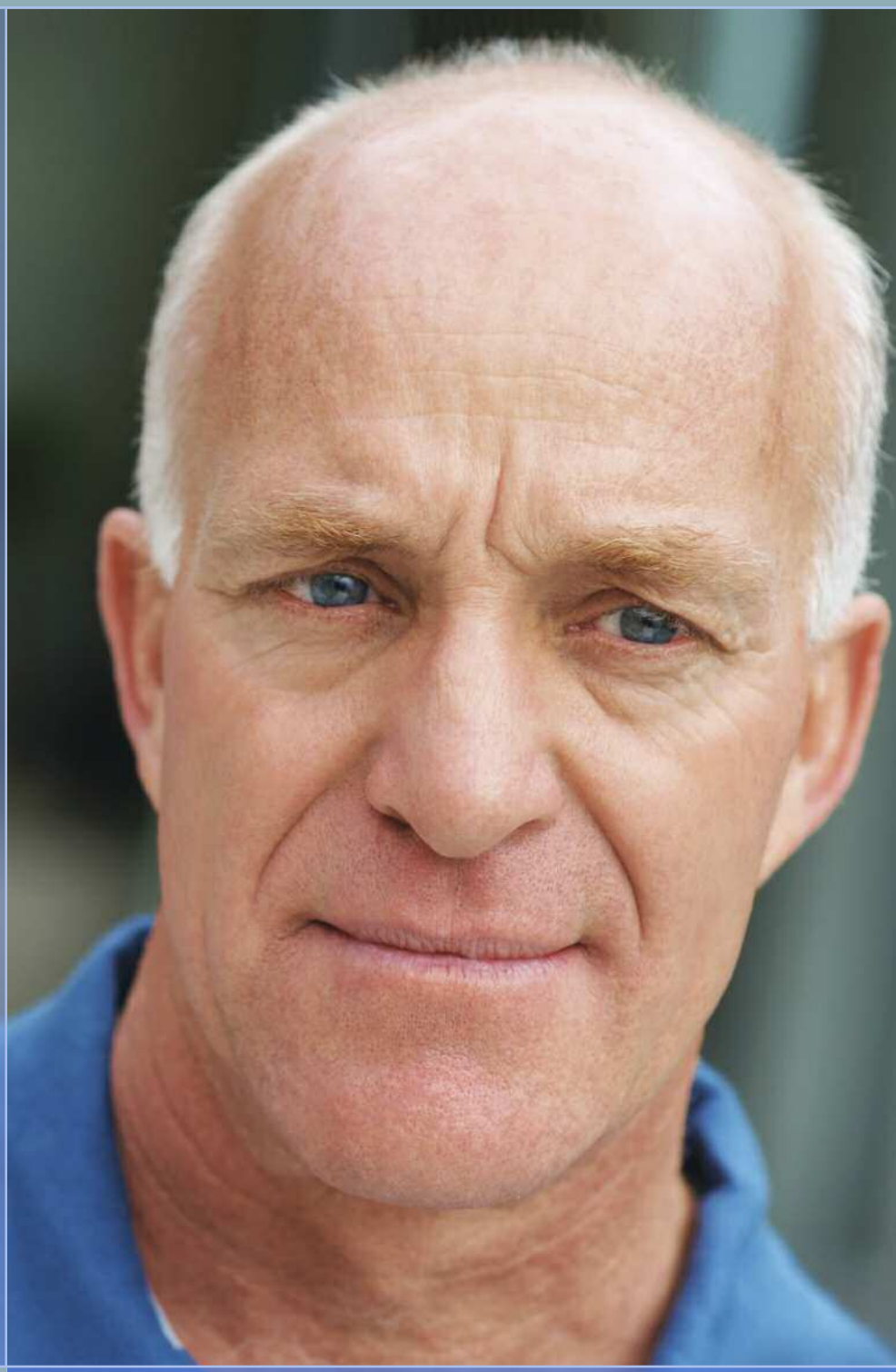
Parkin

PINK1

LRRK2 Full Gene Sequencing

DJ1 Sequencing and Deletion

SNCA Sequencing and Duplication



New Tests Now Available.

athena diagnostics®

Testing that Makes a Difference.

Molecular testing services for

Parkinson's Disease

Athena Diagnostics now offers comprehensive testing for Parkinsonism for all diseases that reflect a dopamine insufficiency in the basal ganglia. These tests identify mutations in the following genes:

Gene	Inheritance	Age of Onset	Associated Phenotypes	Treatment Notes
Parkin (PARK2)[1]	AR	Highly variable; < 40 yrs – 60 yrs	Bradykinesia and tremor are the most common presenting signs. Dystonia is observed in 42% of affected individuals. The clinical signs at examination are also variable, although 44% have hyperreflexia. Abnormal behavior and/or psychiatric manifestations are common and may appear before the onset of parkinsonism [Khan, et al., 2003]. Dementia is rarely observed.	The response to levodopa is better and the incidence of levodopa-induced dyskinesia greater in individuals with parkin-type Parkinson's disease than in those with parkinsonism of different etiologies.
PINK1 (PARK6)[2]	AR	Highly variable; usually < 40 yrs	Bradykinesia and tremor are the most common presenting signs. In some individuals the symptoms at onset are symmetric. Dystonia and hyperreflexia may also be present. In addition to parkinsonism, abnormal behavior and/or psychiatric manifestations are common, in particular depression and anxiety, which occur in about 30% and 15%, respectively. Other features include hallucinations and dementia.	On average, the response to levodopa is better than in other forms of Parkinson's disease; however, the incidence of levodopa-induced dyskinesias may be greater in individuals with *PINK1*-associated Parkinson's disease than in those with parkinsonism of different etiologies.
LRRK2 (PARK8)[3]	AD	28 – 82 yrs	Characterized by features consistent with idiopathic Parkinson's disease: initial motor features of asymmetric tremor at rest and/or bradykinesia, cog-wheel muscle rigidity, postural instability and gait abnormalities including festination and freezing.	*LRRK2* mutations present a slower progression than *SNCA*, without dementia. While these patients respond well to some PD therapy, neuroleptic treatment might advance parkinsonism.[2]
DJ1 (PARK7)[4]	AR	20 – 40 yrs of age	Clinically similar to Parkin; slowly progressive parkinsonism, dystonia and psychiatric abnormalities.	
SNCA (PARK1)[5]	AD	Variable; usually < 50 yrs of age	Rapid progression; often presents with dementia and cognitive decline, and sometimes with atypical features such as central hypoventilation and myoclonus.	Initially good response to levodopa.

Why Test for Genetic Forms of Parkinson's Disease?

- Identify specific gene mutations to clarify best treatment approach
- Eliminate the need for additional testing, such as repeated MRIs and PET scans, to rule out multiple system atrophy
- Establish treatment options of psychogenic symptoms
- Determine need for genetic counseling

Athena Diagnostics Offers the Most Comprehensive Testing for Genetic Forms of Parkinson's Disease

The Complete Parkinsonism Evaluation is Recommended for any Patient with:

- Juvenile onset parkinsonism, regardless of family history
- Early onset parkinsonism with atypical features
- Early onset parkinsonism with a positive family history
- Late onset parkinsonism with a strong family history

The symptoms of Parkinson's plus syndromes (PPS)—or atypical syndromes—respond differently to common Parkinson's disease (PD) therapies and drugs. So, although a cure has yet to be found, an accurate differential diagnosis is essential to properly managing the disease. About 15 percent of PD diagnoses include one of the PPS.

- Corticobasal degeneration
- Lewy body dementia
- Multiple system atrophy
- Progressive supranuclear palsy

PD Differentials and Treatment

With the differential diagnosis afforded by Athena Diagnostics' genetic testing, you can determine the best course of treatment for the presenting symptoms.

Levodopa, for example, is frequently used to treat PD, however, it is largely ineffective in PPS patients who experience either a minimal response or none at all. In fact, cognition may actually worsen as a result of dopaminergic drugs.[6]

Surgical treatments such as deep brain stimulation that are used for some PD cases are also not appropriate for PPS patients.

Athena's Advancement: *LRRK2* Full Gene Sequencing

The *LRRK2* gene has been determined as a key factor in familial PD. The child of a parent with *LRRK2*-related PD has a 50 percent chance of inheriting the gene mutation. This particular gene has been identified with seven pathologic variants, however, at least 100 other coding variants have been observed.[3]

Athena Diagnostics upgraded the *LRRK2* test to full gene sequencing. This major advancement in genetic testing for PD will help uncover and classify variants as pathogenic or benign—which could lead to invaluable insights for future treatment and insights into the disease itself.

The PD Population

- Parkinson's disease affects seven to ten million people around the world and about one million in the U.S.—more than the total cases of people diagnosed with multiple sclerosis, muscular dystrophy, and ALS.[7]
- Although over 60,000 Americans are diagnosed with PD every year, it is likely that thousands of cases go undetected.[3]
- Approximately four percent of PD cases are diagnosed in patients under the age of 50.[3]
- One percent of the people over the age of 55 and three percent of those over 75 will be diagnosed with PD.[3]
- Men are one and a half times more likely than women to have PD.[3]
- Twenty percent of patients with parkinsonism also present with dementia.

15 to 20 Percent of PD Patients have a Clear Positive Family History.[8]

Comprehensive Services from Athena Diagnostics

Athena Insight™

Athena Insight is a powerful result-reporting service that is included with every DNA sequencing test ordered. Our technical comprehensive review of variants of unknown significance determines the likelihood of variants being benign or pathogenic. A complete synopsis of research data and findings is presented in clear and concise clinical terms enabling the physician to utilize this enhanced report with patients and family members during discussions relative to diagnosis, treatment, patient management and family planning.

Genetic Counselors at Your Service

Genetic Counselors can provide information on the nature, inheritance and implications of genetic disorders to help the physician guide the patient and family in making informed medical and personal decisions.

Athena's Test Menu for Parkinson's Disease

Test Code	Test Name	Specimen Volume Tube Type	Turnaround Time
588	Complete Parkinsonism Evaluation *(LRRK2, Parkin, PINK1, DJ1, SNCA)*	10 mL whole blood, lavender top tube	21 – 28 days
558	*LRRK2* DNA Sequencing Test	10 mL whole blood, lavender top tube	21 – 28 days
559	PARK2 *(Parkin)* DNA Sequencing Test	10 mL whole blood, lavender top tube	21 – 28 days
040	PARK2 *(Parkin)* Duplication/Deletion Test	10 mL whole blood, lavender top tube	21 – 28 days
542	*PINK1* DNA Sequencing Test	10 mL whole blood, lavender top tube	21 – 28 days
058	*PINK1* Deletion Test	10 mL whole blood, lavender top tube	21 – 28 days
554	PARK7 *(DJ1)* DNA Sequencing Test	10 mL whole blood, lavender top tube	21 – 28 days
047	PARK7 *(DJ1)* Deletion Test	10 mL whole blood, lavender top tube	21 – 28 days
557	Alpha Synuclein *(SNCA)* DNA Sequencing Test	10 mL whole blood, lavender top tube	21 – 28 days
059	Alpha Synuclein *(SNCA)* Duplication/Deletion Test	10 mL whole blood, lavender top tube	21 – 28 days

Client Services Representatives are available from 8:30am to 6:30pm Eastern Time (U.S.). Customers in the U.S. and Canada please call toll free **800-394-4493** or visit us on our website at **AthenaDiagnostics.com.**

athena diagnostics®

Testing that Makes a Difference.

References: 1. Brice A, Dürr A, Lücking C. Parkin Type of Juvenile Parkinson Disease. 2001 Apr 17 [Updated 2007 Oct 1]. In: Pagon RA, Bird TD, Dolan CR, et al., editors. *GeneReviews*™ [Internet]. Seattle (WA): University of Washington, Seattle; 1993-. Available from: http://www.ncbi.nlm.nih.gov/books/NBK1478/. 2. Schneider SA, Klein C. PINK1 Type of Young-Onset Parkinson Disease. 2010 Mar 16. In: Pagon RA, Bird TD, Dolan CR, et al., editors. *GeneReviews*™ [Internet]. Seattle (WA): University of Washington, Seattle; 1993-. Available from: http://www.ncbi.nlm.nih.gov/books/NBK26472/. 3. Farrer M, Ross OA. LRRK2-Related Parkinson Disease. 2006 Nov 2 [Updated 2010 Apr 29]. In: Pagon RA, Bird TD, Dolan CR, et al., editors. *GeneReviews*™ [Internet]. Seattle (WA): University of Washington, Seattle; 1993-. Available from: http://www.ncbi.nlm.nih.gov/books/NBK1208/. 4. Crosiers, D. *Journal of Chemical Neuroanatomy* 42 (2011) 131-141. 5. Klein, Christine and Ana Westenberger. *Cold Spring Harb Perspect Med* 2012; 2:a008888. 6. Parkinson's Disease Foundation, "Understanding Parkinson's Plus Syndromes and Atypical Parkinsonism." 7. Parkinson's Disease Foundation, Statistics on Parkinson's, accessed 4/17/12, http://www.pdf.org/en/parkinson_statistics. 8. Nuytemans, Karen, Theuns, Jessie, Cruts, March, and Van Btoeckhoven, Christine, "Genetic Etiology of Parkinson Disease Associated with Mutations in the *SNCA, PARK2, PINK1, PARK7,* and *LRRK2* Genes: A Mutation Update," *Human Mutation,* Vol. 31, No. 7, 763-780, 2010.

ADX448SG-9/12SR-REV00