

# Genetic Testing FAQs



## What are the benefits of genetic testing?

Genetic tests can help to:

- Diagnose disease
- Improve the accuracy of a patient's prognosis and genetic counseling
- Identify gene mutations that could be passed on to children
- Screen newborn babies for certain treatable conditions
- Identify mutations presymptomatically. For some diseases, including early-onset glaucoma, this allows for increased disease surveillance and timely treatment.

## What is required for a genetic test?

Genetic testing requires a tissue sample from the patient, usually blood or saliva, which is sent to a CLIA-certified laboratory for testing.

## What factors should I consider before ordering a test?

- **Usefulness:** Consider whether or not testing will help you better manage your patient, including the opportunity for gene-based therapies as they become more readily available. Genetic testing is particularly useful for patients who have a family history of inherited retinal degenerations, early-onset glaucoma, and primary optic atrophy.
- **Cost:** For many patients, affordability is an important consideration and should be factored in to the decision-making process. Costs versus benefits also should be considered. In some cases, an expedited test result (a more expensive option) may allow more rapid access to effective therapy or to information that is needed for family planning. At Mass. Eye and Ear, costs range from \$500 to \$3,500 depending on the type of test. Health insurance may cover part or all of the costs.
- **Turnaround Time:** This varies laboratory to laboratory, and will depend upon the type of test ordered. Typical turnaround time at Mass. Eye and Ear is 90 days.
- **Reporting:** Patients should receive written copies of each genetic test report. Reports are returned to the physician who ordered the test and should be interpreted by a health care provider with knowledge of the disease genetics.

FIRST CLASS  
U.S. POSTAGE  
PAID  
PERMIT NO. 51711  
BOSTON, MA



243 Charles Street  
Boston, MA 02114  
MassEyeAndEar.org

eye Insights™

# Genetic Testing

Sensitive and specific genetic tests now exist for dozens of inherited eye diseases. So, what tests are available, and when are they appropriate for your patients?

## Inside:

- Are your patients ready for genetic testing?
- General guidelines for genetic testing
- Genetic testing services at Mass. Eye and Ear
- Frequently asked questions about genetic testing

Dear Colleagues:

The accelerated pace of molecular discoveries during the past two decades, coupled with an evolving “precision medicine” model in healthcare, are fueling an increase in the number of people who undergo genetic testing.



In Ophthalmology, genetic testing is still in its early stages, but already is transforming our ability to pinpoint the cause of some inherited eye diseases that result from single gene mutations, such as retinitis pigmentosa. In many cases, genetic testing can help your patients and their families better understand their risk for disease, likelihood of disease progression, and options for treatment. It can also help them make more informed decisions about their health.

Sensitive and specific genetic tests now exist for dozens of inherited eye diseases. In this issue of

*Eye Insights* we explore what tests are available, and provide guidelines for assessing when genetic testing may benefit your patients and how it can be incorporated into your clinical care practice.

The Harvard Medical School Department of Ophthalmology Ocular Genomics Institute (OGI), based at Massachusetts Eye and Ear, offers comprehensive genetic diagnostic testing for inherited eye diseases, including inherited retinal degenerations, early-onset glaucoma, and primary optic atrophy, via several Genetic Eye Disease (GEDI) tests. As described in a paper published in the journal *Genetics in Medicine*, analyses performed by the OGI team show that GEDI testing provides more accurate diagnoses than other testing methods; this can improve genetic counseling and facilitate the use of focal ocular treatments and therapies, including gene therapies. Our service is CLIA-certified, and we invite you to learn more by visiting [MassEyeAndEar.org/genetictesting](http://MassEyeAndEar.org/genetictesting).

Joan W. Miller

Joan W. Miller, MD  
Henry Willard Williams Professor of Ophthalmology  
Chair, Harvard Medical School Department of Ophthalmology  
Chief of Ophthalmology, Massachusetts Eye and Ear and  
Massachusetts General Hospital

## SAVE THE DATE

4<sup>th</sup> Biennial International Symposium on AMD  
and  
2<sup>nd</sup> Biennial Symposium on Ocular Regeneration

October 20-22, 2016 | Boston, MA

For more information, please visit:  
[eye.hms.harvard.edu/AMD2016](http://eye.hms.harvard.edu/AMD2016)



eye Insights™



## When is genetic testing appropriate?

Many inherited diseases are caused by mutations in a single gene (Mendelian disorder), and detection of the responsible mutation can predict development of the disease with relatively high accuracy. If your clinical findings suggest the presence of an inherited eye disease, such as those described below, genetic testing is worth considering and discussing with your patient.

Some heritable disorders are complex, meaning that they are the result of multiple genetic and environmental factors. The presence of any one of the disease-associated gene variants in complex disorders, such as age-related macular degeneration, may not be highly predictive of the development of the disease. In these cases, standard diagnostic methods such as biomicroscopy, ophthalmoscopy, tonography, and perimetry – rather than genetic testing – will more accurately assess a patient's risk of vision loss.

### Inherited Retinal Degenerations

Patients with clinical features of inherited retinal degenerations can benefit from genetic testing. Identifying disease-causing mutations aids genetic counseling by establishing the inheritance pattern (autosomal dominant, recessive, X-linked, or mitochondrial [maternal] inheritance), and identifying patients who are eligible to take part in clinical trials evaluating gene-based and cellular therapies. Many patients with inherited retinal degenerations have similar clinical features. For this reason, the GEDi-R panel is the most efficient method of screening, simultaneously testing 250 genes known to cause retinal degenerations.

### Early-onset Glaucoma

When glaucoma develops in a patient before age forty (early-onset glaucoma), the disease is more likely to be caused by one of eight known high-risk genes. Early-onset glaucoma genes contribute to a broad range of phenotypes that can be difficult to distinguish by clinical features alone. The most efficient method to screen for early-onset glaucoma gene mutations is to use a panel test, such as GEDi-O, that simultaneously screens all eight genes. This information can aid genetic counseling by defining the inheritance pattern and identifying mutation carriers presymptomatically.

### Primary Optic Atrophy

Approximately 50 percent of patients with primary optic atrophy have disease-causing mutations in either the *OPA1* gene (inherited as a dominant trait and causing Kjer optic neuropathy), or mitochondrial DNA (inherited through maternal lineage and causing Leber Hereditary Optic Neuropathy). Nine other gene variants with dominant or recessive inheritance traits are also known to cause optic atrophy. Therefore, identifying the patient's disease-causing genes will help define the inheritance pattern and phenotype. Since primary optic atrophy can overlap phenotypically with the normal tension type of glaucoma, it is useful to screen patients for both optic atrophy and glaucoma genes using the GEDi-O panel test. Additionally, clinical trials of gene therapy for specific genetic forms of optic neuropathy are in progress; genetic testing can help determine if patients are eligible for these studies.

For further reading, please see: Wiggs JL, Pierce EA. Genetic testing for inherited eye disease: who benefits? *JAMA Ophthalmol*. 2013 Oct;131(10):1265-6.

## General Guidelines for Genetic Testing

- ✓ Offer genetic testing to patients whose clinical findings suggest a Mendelian disorder with a known gene mutation.
- ✓ If you are unfamiliar with the specific testing required, encourage the involvement of a board-certified medical geneticist, genetic counselor, or both for all genetic tests. This will help to ensure accuracy of testing and interpretation of results, and that proper counseling is provided to the patient.
- ✓ Use Clinical Laboratories Improvement Amendments (CLIA)–approved laboratories for all clinical testing to ensure accuracy and quality of testing.
- ✓ Provide a copy of each genetic test report to the patient. This information allows patients to independently search for mechanism-specific information, such as the availability of gene-specific clinical trials.
- ✓ Consider panel testing for disorders that can be caused by mutations in more than one gene.
- ✓ Avoid direct-to-consumer genetic testing and discourage patients from obtaining such tests themselves.
- ✓ Avoid routine genetic testing for genetically complex disorders like age-related macular degeneration and late-onset glaucoma.
- ✓ Avoid testing asymptomatic minors for untreatable disorders except when surveillance or lifestyle modifications can be beneficial.

Adapted from: Stone EM, Aldave AJ, Drack AV, Maccumber MW, Sheffield VC, Traboulsi E, Weleber RG. Recommendations for genetic testing of inherited eye diseases: report of the American Academy of Ophthalmology task force on genetic testing. *Ophthalmology*. 2012 Nov;119(11):2408-10.

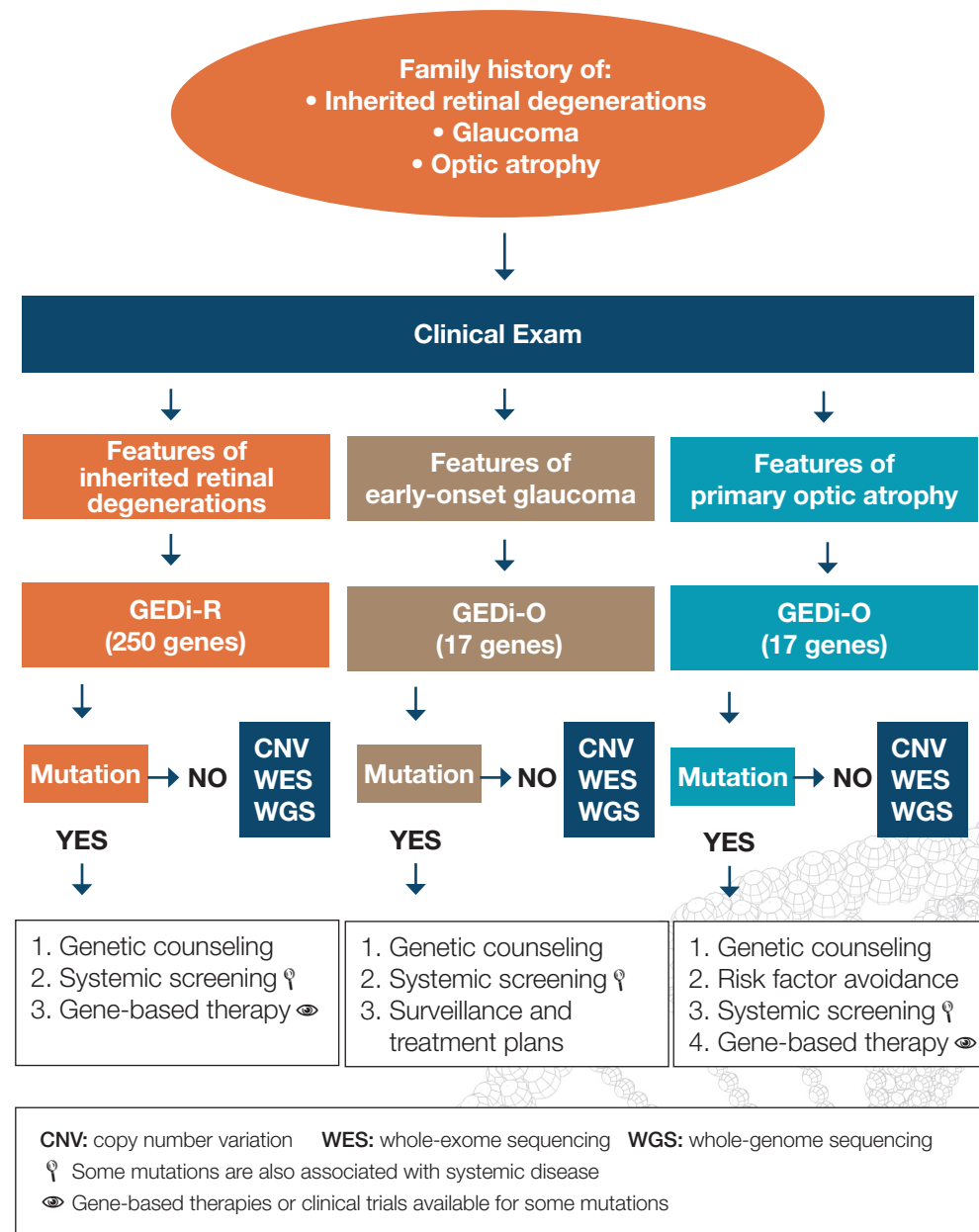
## Genetic Testing Services at Mass. Eye and Ear

Genetic testing can be ordered only by a medical professional. Blood is the preferred specimen for testing. CLIA-certified genetic testing services provided by the Ocular Genomics Institute at Mass. Eye and Ear range from \$500-\$3,500. Health insurance may cover part or all of the cost. A typical turnaround time is 90 days.

- Genetic Eye Disease panel for Retina genes (GEDi-R) - Inherited retinal degenerations and related disorders
- Genetic Eye Disease panel for Optic nerve genes and early onset glaucoma (GEDi-O)
- Genetic Eye Disease panel for Strabismus genes (GEDi-S)
- Confirmation of research finding or familial variant testing

**For inquiries and test requisition forms:**  
**MassEyeAndEar.org/geneticTesting**  
**Tel: 617-573-6906**

## Integrating Genetic Testing into Clinical Care



The Ocular Genomics Institute at Mass. Eye and Ear translates genomic medicine into precision ophthalmic care by facilitating and promoting genomics and gene therapy research in the Harvard Medical School Department of Ophthalmology.

## Meet the Experts



### Janey Wiggs, MD, PhD

Associate Director of the Ocular Genomics Institute at Mass. Eye and Ear

Paul Austin Chandler Professor of Ophthalmology at Harvard Medical School

Dr. Wiggs is a board-certified medical geneticist specializing in the genetics of glaucoma with particular interest in complex and advanced glaucoma, and inherited ocular disorders. She directs the CLIA-certified clinical diagnostic genetic laboratory at Mass. Eye and Ear, where patients are tested for mutations in genes that can cause inherited retinal disorders, early-onset glaucoma, or primary optic neuropathy.



### Eric Pierce, MD, PhD

Director of the Ocular Genomics Institute at Mass. Eye and Ear

Sol and Libe Friedman Associate Professor of Ophthalmology at Harvard Medical School

Dr. Pierce seeks to improve our understanding of the molecular bases of inherited retinal degenerations so that rational therapies can be developed for these diseases. As a clinician scientist, he conducts clinical research and laboratory-based investigations of retinal biology and disease, and provides clinical care for children and adults with retinal degenerative disorders. He is currently working to develop gene therapy for several forms of inherited retinal degenerations.

### Related Reading

1. Stone EM, Aldave AJ, Drack AV, Maccumber MW, Sheffield VC, Traboulsi E, Weleber RG. Recommendations for genetic testing of inherited eye diseases: report of the American Academy of Ophthalmology task force on genetic testing. *Ophthalmology*. 2012 Nov;119(11):2408-10.
2. Wiggs JL, Pierce EA. Genetic testing for inherited eye disease: who benefits? *JAMA Ophthalmol*. 2013 Oct;131(10):1265-6.

## eye Insights™ February 2016

Editor-in-Chief:  
Joan W. Miller, MD

Managing Editor:  
Matthew F. Gardiner, MD

Communications Director:  
Suzanne Ward

Clinical Advisory Group:  
Carolyn E. Kloek, MD  
Deeba Husain, MD  
Ankoor S. Shah, MD, PhD  
Angela V. Turalba, MD

Scientific Communications Manager:  
Wendy Chao, PhD

Publications Manager:  
Wendy Weissner

Graphic Design:  
Beth Durkee

Contributors: Janey Wiggs, MD, PhD, and Emily Place, MS, LCGC

Published biannually, *Eye Insights™* offers the ophthalmology community best practice information from Mass. Eye and Ear specialists with each issue focused on a specific disease topic. We welcome your feedback. Send comments to: [eyeinsights@meei.harvard.edu](mailto:eyeinsights@meei.harvard.edu).

