Interpreting genetic tests: The basics of molecular diagnosis through application of results

# Course organizers

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**Robert Hufnagel, MD, PhD**, National Institutes of Health (NIH)  
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# Presentations

Presenters and presentations may change.

| **Time** | **Topic** | **Speaker** |
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| 1-1:30pm | Phenotyping inherited ocular diseases in the era of genetic testing & therapy | Ramiro Maldonado, MD.  Duke University Eye Center  <https://www.dukehealth.org/find-doctors-physicians/ramiro-s-maldonado-md> |
| Structural and functional testing of inherited ocular diseases has significantly improved over the years. Knowing when to order and how to interpret testing to obtain deep phenotyping while maintaining an efficient clinic is extremely important. This presentation will cover the most recent advances in ophthalmology applicable to the evaluation of inherited ocular diseases with practical examples. | | |
| 1:30-2pm | Gene 101. Basics of molecular diagnostics | Robert Hufnagel, MD, PhD.  National Institutes of Health (NIH)  <https://www.nei.nih.gov/research/research-labs-and-branches/we-are-nei-intramural/robert-hufnagel> |
| This presentation will cover basic terminology including nomenclature for genetics and genomics. A brief history of molecular diagnostic testing will be followed by state of the art clinical and research genetic testing methods, including comparisons of different technologies and sequencing approaches. Finally, sequence data analysis will be described. | | |
| 2-2:30pm | Genetic counseling in Ophthalmology | Kari Branham, MS, CGC  University of Michigan  <https://medicine.umich.edu/dept/ophthalmology/kari-branham-ms-cgc> |
| Genetic counseling is an essential aspect of the clinical care and management of patients affected with inherited eye diseases. During this portion of the education course, we will review essential elements of a genetic counseling session and discuss the value genetic counseling and genetic testing can provide for both patients and their health care providers. Moreover, we will discuss different models for the integration of genetic counselors into the care of patients with inherited eye disease. Case examples will be presented to illustrate these points. | | |
| 2:30-3pm | Interpreting genetic test results for ocular disorders: The basics of molecular diagnosis through application of results | Kristy Lee, MS, CGC.  University of North Carolina (UNC)  <https://www.med.unc.edu/genetics/directory/kristy-lee/> |
| Genetic testing options for ocular disorders are expanding and becoming more widely used in clinical care. However, genetic testing results are not always easy to interpret or informative. This presentation will provide a basic overview on how gene variants are evaluated for pathogenicity, as well as highlight some of the challenges and pitfalls with interpreting genetic testing results and offer guidance on sharing results with patients. | | |
| 3-3:15pm | Break |  |
| 3:15-3:45pm | ClinGen gene: Disease and variant curation | Gavin Arno  Moorfields Eye Hospital  <https://www.ucl.ac.uk/ioo/people/dr-gavin-arno> |
| The genomic revolution and widespread availability of next generation sequencing for rare diseases has driven genetic discovery for more than a decade and now dominantes molecular diagnostic practice. With these advances in our ability to detect rare variants across the entire genome comes increased uncertainty of the impact of many variants and genotypes. Standardization of variant interpretation (ACMG/AMP guidelines) often leads to uncertainty (variants of uncertain significance) and the importance for many genes in disease is unclear. The overall aim of the ClinGen Gene Curation Expert Panels (GCEP) and the Variant Curation Expert Panels (VCEP) is to provide gene and variant level expert guidance for interpretation of genetic results for clinicians, clinical scientists, molecular geneticists and counsellors. Here, we will explore the process of gene and variant curation with case studies to highlight some of the challenges. | | |
| 3:45-4:15pm | Public databases and Sponsored testing programs | Emily Place, MS, LCGC  MEEI-Harvard  <https://oculargenomics.meei.harvard.edu/labs/genetic-counseling/team-members/> |
| Sharing of genetic data is critical to further our understanding of mendelian disease and improve interpretation of genetic results. This talk will discuss data sharing in the different yet equally important areas of sponsored genetic testing programs and public variant databases. We will discuss aspects of each area, highlight benefits and limitation of each and discuss useful ways to share data while protecting the identity of patients. | | |
| 4:15-4:45pm | Expecting the unexpected: incidental and secondary findings in genetic testing | Linda Reis, MS, CGC  Medical College of Wisconsin  <https://www.mcw.edu/departments/pediatrics/divisions/developmental-biology/research/semina-laboratory> |
| The use of next generation sequencing, through panel, exome, and/or genome testing is often the most efficient method to identify causative variants in genetically heterogeneous ocular disorders. However, broad testing can reveal unexpected results. Conversely, exome sequencing for other indications may identify an incidental diagnosis of an unrecognized ocular condition. This presentation will review the range of incidental and secondary findings or unexpected diagnoses that may be returned from clinical testing. | | |
| 4:45-5pm | Panel Q&A |  |
| Open discussion with the speakers. | | |
| 5pm | Adjourn |  |