2017 | ACMG Annual Clinical Genetics Meeting

ACMG American College of Medical Genetics and Genomics
Translating Genes Into Health®

Platform Presentations - Neurogenetics

Held in Phoenix, Arizona, March 21-25, 2017

Date of Release: April 3, 2017
Expiration Date: April 3, 2020 (CME, NSGC, P.A.C.E.®)
Estimate Time of Completion: 2 hours
Course must be completed by the expiration dates

COURSE DESCRIPTION

ACMG's Program Committee has assembled abstract-driven platform talks. Each presenting author will give a 10-minute talk followed by 5 minutes of discussion.

LEARNING OBJECTIVES

At the conclusion of this course, participants should be able to:

- Review the genes that were identified through diagnostic exome sequencing in patients who have epilepsy
- Recognize the clinical utility of GDF15 levels in mitochondrial disease
- Illustrate the clinical utility of whole exome sequencing as a diagnostic tool for ataxia-related disorders
- Compare the diagnostic yield of chromosomal microarrays and clinical exome sequencing in autism cases
- Describe a novel intellectual disability syndrome
- Classify development brains disorders candidate genes using an evidence-based, cross-disorder approach
- Describe the phenotype associated with PBX1 variants in humans

TARGET AUDIENCE

All healthcare professionals interested in the diagnosis, management, treatment and prevention of genetic conditions and increasing their understanding of the genetic basis of common, chronic health problems affecting both children and adults will find the programming applicable to their practice. These select sessions from the ACMG Annual Meeting are targeted for the following professionals:

- Medical and clinical geneticists
- Physicians of all specialties with an interest in genetics, genomics and the genetic basis of disease
- Genetic counselors
- Laboratory geneticists, directors, technicians and technologists
- Researchers

- Pathologists
- Educators
- Nurses
- Dietitians
- Physician assistants
- Biotechnology and pharmaceutical development professionals
- Fellows, Trainees and Students
- Public health professionals
- Genetic/consumer advocates
- Others with an interest in the science and art of medical genetics and genomics

SESSIONS

- Diagnostic Utility of Clinical Exome Sequencing in Autism Spectrum Disorder [Abstract Number: 45] Sureni Mullegama, PhD, ABMGG Clinical Molecular Genetics Fellow (Presenting Author)
- Diagnostic Exome Sequencing in a Cohort of Adult and Pediatric Epilepsy Patients [Abstract Number: 46] Natalie Lippa, MS, CGC (Presenting Author)
- Exome Sequencing Provides a Broad Evaluation and High Diagnostic Rate for Ataxia-Related Disorders [Abstract Number: 47] Sujatha Sastry, MS, CGC (Presenting Author)
- Development of an Evidence-Based Gene Database for Developmental Brain Disorders [Abstract Number: 48] Andrea Gonzalez Mantilla, MD (Presenting Author)
- *De novo*, Deleterious Sequence Variants in *PBX1* are Associated with Developmental Differences, Branchial Arch Anomalies and Renal Abnormalities [Abstract Number: 49] Anne Slavotinek, MBBS, PhD, FACMG (Presenting Author)
- Biallelic Loss-of-Function Variants in *OTUD6B* Cause an Intellectual Disability Syndrome Associated with Seizures, Microcephaly, Absent Speech, Hypotonia, and Growth Retardation [Abstract Number: 50] Teresa Santiago-Sim, PhD (Presenting Author)
- Clinical Testing for Growth Differentiation Factor 15 (GDF15), a Potential Biomarker of Mitochondrial Disease [Abstract Number: 51] Devin Oglesbee, PhD (Presenting Author)

Accreditation:

The American College of Medical Genetics and Genomics is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

Credit Designation:

The American College of Medical Genetics and Genomics designates this activity for a maximum of 2 *AMA PRA Category 1 Credit*s™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Genetic Counselor Credit

The National Society of Genetic Counselors (NSGC) has authorized American College of Medical Genetics and Genomics to offer up to 2 Category 1 contact hours for this OnDemand course. The American Board of Genetic Counseling (ABGC) will accept CEUs earned for this course for the purposes of genetic counselor certification and recertification. Reporting of credits is sent to NSGC quarterly. Additional fee (~$25) applies for NSGC credit that is billed by NSGC.

P.A.C.E. CEUs – Laboratory Directors and Laboratory Personnel

ACMG is approved as a provider of continuing education programs in the clinical laboratory sciences by the American Society for Clinical Laboratory Science (ASCLS) Professional Acknowledgment for Continuing Education (P.A.C.E.®) Program. The American College of Medical Genetics and Genomics designates this course for a maximum of 2 contact hours. ACMG is approved by the Florida Board of Clinical Laboratory Personnel as CE Provider. ACMG is approved by the California Department of Health Services through the ASCLS P.A.C.E.® Program as CE Provider #275.

HIPAA Compliance

The ACMG supports medical information privacy. While the ACMG is not a "covered entity" under HIPAA 1996 and therefore is not required to meet these standards, ACMG wishes to take reasonable steps to ensure that the presentation of individually identifiable health information at ACMG-sponsored events has been properly authorized. All presenters have completed a form indicating whether they intend to present any form of individually identifiable healthcare information. If so, they were asked either to attest that a HIPAA-compliant consent form is on file at their institution, or to send ACMG a copy of the ACMG HIPAA compliance form. This information is on record at the ACMG Administrative Office and will be made available on request.

Content Validation

ACMG follows the ACCME policy on Content Validation for CME activities, which requires:

Content Validation and Fair Balance

1. ACMG follows the ACCME policy on Content Validation for CME activities, which requires:
   a) All recommendations involving clinical medicine must be based on evidence that is accepted within the profession of medicine as adequate justification for their indications and contraindications in the care of patients.
   b) All scientific research referred to, reported or used in CME in support or justification of patient care recommendations must conform to the generally accepted standards of experimental design, data collection and analysis.

2. Activities that fall outside the definition of CME/CE; "Educational activities that serve to maintain, develop, or increase the knowledge, skills, and professional performance and relationships that a physician uses to provide services for patients, the public, or the profession" (source: ACCME and AMA) will not be certified for credit. CME activities that promote recommendations, treatment, or manners of practicing medicine or pharmacy that are not within the definition of CME/CE or, are known to have risks or dangers that outweigh the benefits or, are known to be ineffective in the treatment of patients.
3. Presentations and CME/CE activity materials must give a balanced view of therapeutic options; use of generic names will contribute to this impartiality. If the CME/CE educational materials or content includes trade names, where available, trade names from several companies must be used.

Off-label Uses of Products

When an off-label use of a product, or an investigational use not yet approved for any purpose, is discussed during an educational activity, the accredited sponsor shall require the speaker to disclose that the product is not labeled for the use under discussion, or that the product is still investigational. Discussions of such uses shall focus on those uses that have been subject of objective investigation.

Disclaimer: *ACMG educational programs are designed primarily as an educational tool for health care providers who wish to increase their understanding of the application of genomic technologies to patient care. The ACMG does not endorse, or recommend the use of this educational program to make patient diagnoses, particular by individuals not trained in medical genetics. Adherence to the information provided in these programs does not necessarily ensure a successful diagnostic outcome. The program should not be considered inclusive of all proper procedures and tests or*

exclusive of other procedures and tests that are reasonably directed at obtaining the same results. In determining the propriety of any specific procedure or test, a healthcare provider should apply his or her own professional judgment to the specific clinical circumstances presented by the individual patient or specimen.

2017 ACMG Program and Education Committee Members Disclosures

Members of the ACMG Staff, Education and Program Committees involved in planning the 2017 ACMG Annual Clinical Genetics Meeting are required to disclose relevant relationships which could be perceived by some as a real or apparent conflict of interest in planning. All disclosures have been reviewed and conflicts of interest resolved by the Education Committee COI sub-committee or the Executive Director and CME Associate Director and conflicts of interest are disclosed. In the cases where a conflict existed then the committee member refrained from the discussion.

Following is a list of program and education committee members who have disclosed one or more such relationships and names of companies with which those relationships exist:

EC = Education Committee; PC = Program Committee; S = ACMG Staff

1. Major stockholder/ownership interest 2. Grant/Research Support (External) 3. Salary/Employment/Royalty(ies)/Honoraria 4. Consultant/consulting fees/other remuneration 5. Speakers' bureau	6. Non-remunerative positions of influence such as officer, board member, trustee, or public spokesperson (All Committee Members Below are on ACMG Committees –Members with other affiliations are listed) 7. Receipt of intellectual property 8. Other

Georgianne L. Arnold, MD, FACMG - Horizon, 2; Recordati, 2; Biomarin, 2; Actelion, 2; SIMD, 6; ACGME, 6; AAP, 6; ASHG, 6 (PC)
Karen W. Gripp, MD, FACMG – Wiley Publishing Inc., 3; FDNA, 4; Novartis, 4 (PC)
Fuki M. Hisama, MD, FACMG – Horizon Pharmaceuticals, 4; ABMGG, 6 (PC)
Christine A. Curtis, PhD, FACMG - CSI Laboratories, 3 (EC)
Thomas E. Mullen, PhD, MS, FACMG - Good Start Genetics Inc., 3 (EC)
Christian P. Schaaf, MD, PhD, FACMG - Springer Publishing Company, 3 (PC), (EC)
Katrina M. Dipple, MD, PhD, FACMG – ACGME, 6; AAP, 6; ASHG, 6; LA BioMed DSMB, 4; SIMD 6 (PC)

Following is a list of committee, education members and staff who have no relationships to disclose:

Liming Bao, PhD, FACMG (EC)
Monica A. Giovanni, MS (EC)
Chad Haldeman-Englert, MD, FACMG (EC)
Abbas Padeganeh, PhD, MS (EC)
Amy E. Roberts, MD, FACMG (EC)
Barrie Suskin Kaplan, MD (EC)
Tracey Weiler, PhD, MS (EC)
Jansson White (EC)
Anne M. Slavotinek, MBBS, PhD, FACMG (EC)
Christopher M. Cunniff, MD, FACMG (PC)
Gerald Feldman, MD, PhD, FACMG (PC)
Helga V. Toriello, PhD, FACMG (PC)
Hope Northrup, MD, FACMG (PC)
Jennelle C. Hodge, PhD, FACMG (PC)
Jessica Smith, MD (PC)
Joanne Nguyen, MD, FACMG (PC)
Myra Wick, MD, PhD, FACMG (PC)
Omar Abdul-Rahman, MD, FACMG (PC)
Pilar L. Magoulas, MS, CGC (PC)
Robert Hagelstrom, PhD, MBA, FACMG (PC)
Tuya Pal, MD, FACMG (PC)
Monica Giovanni, MS, CGC (PC)
Jane Dahlroth, CEM, CMP-HC (PC), (EC), (S)
Jane Radford, MHA, CHCP (PC), (EC), (S)
Michael S. Watson, PhD, FACMG (PC), (EC), (S)
Penelope Freire, CMP (PC), (S)

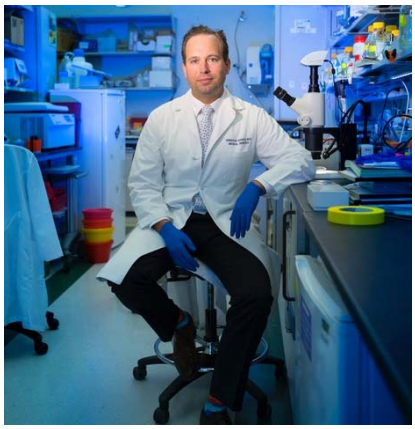
SPEAKERS AND MODERATORS

As a sponsor accredited by the ACCME, the American College of Medical Genetics and Genomics must ensure balance, independence, objectivity and scientific rigor in all its sponsored educational activities. All faculty participating in a CME-certified activity are expected to disclose to the audience any relevant financial interest(s) or other relationship(s) with the manufacturer(s) of any commercial product(s), provider(s) of commercial services or any commercial supporters, including diagnostic laboratories, of the activity discussed in an educational presentation. Relevant financial interest(s) or other relationship(s) can include such things as grants or research support, consultancy, major stock holder, etc. The intent of this disclosure is not to prevent a planner or speaker with a relevant financial or other relationship from course planning or making a presentation, but rather to provide learners with information on which they can make their own judgments. It remains for the audience to determine whether the speaker's interests or relationships may influence the presentation with regard to exposition or conclusion. All conflicts of interests have been reviewed and resolved by the education and CME subcommittee.

Moderator: Liming Bao, MD, PhD, FACMG
Professor, Department of Pathology and Laboratory Medicine, Geisel School of Medicine Dartmouth College
No financial relationships to disclose.

Liming Bao, MD, PhD, is Professor of Pathology and Laboratpory Medicine and the Medical Director of Cytogenetics Laboratory at Dartmouth-Hitchcock Medical Center and Geisel School of Medicine at Dartmouth College, and the Medical Director of Clinical Laboratory at the New London Hospital in New Hampshire. Before joining the Dartmouth-Hitctchcook Medical Center, he was the Associate Director of Cytogenetics Laboratory at the Cincinnati Children's Hospital Medical Center. He is board certified in cytogenetics and clinical molecular genetics by the American Board of Medical Genetics and Genomics. His research interests are cancer genomics and genetic etiology of inherited disorders.

Moderator: Christian Schaaf, MD, PhD, FACMG, ABMGG
Assistant Professor, Baylor College of Medicine
No financial relationships to disclose.



Christian is an assistant professor in the Department of Molecular and Human Genetics of Baylor College of Medicine and an investigator at the Jan and Dan Duncan Neurological Research Institute of Texas Children's Hospital. Christian has been remarkably successful as a physician, scientist, and educator. He and his team have discovered several new disease genes for neurodevelopmental disorders, including those for Schaaf-Yang syndrome and Bosch-Boonstra-Schaaf Optic Atrophy syndrome. Christian's work has been recognized with numerous awards, including a Doris Duke Clinical Scientist Development Award, the Physician Scientist Award by the Chao Foundation, the prestigious William K. Bowes Jr. Award in Medical Genetics, and the Donald Seldin – Holly Smith Award for Pioneering Research by the American Society for Clinical Investigation. Christian has authored four books, including

a major textbook of medical genetics. Christian currently serves as the Chair of Education for the American College of Medical Genetics.

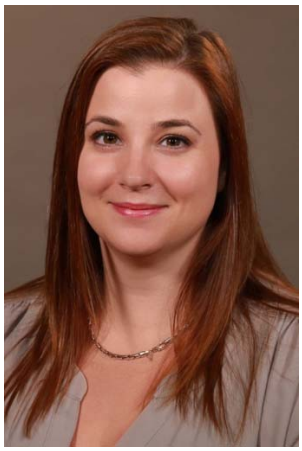
Moderator: Helga V. Toriello, PhD, FACMG
Spectrum Health
No financial relationships to disclose.

Dr. Toriello currently hold a position with Michigan State University on administration and teaching faculty. Also see patients occasionally at Spectrum Health

Speaker: Sureni Mullegama, PhD, ABMGG Clinical Molecular Genetics Fellow
UCLA, Departments of Pathology and Laboratory Medicine and UCLA Clinical Genomics Center
No financial relationships to disclose.

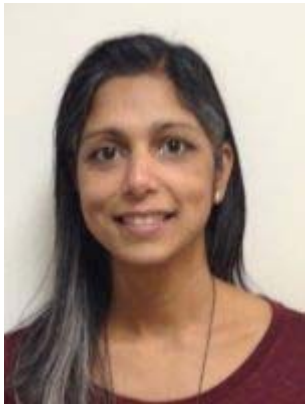
Dr. Sureni V. Mullegama is currently completing her last year of her ABMGG Clinical Molecular Genetics Fellow at the UCLA Intercampus Medical Genetics Training Program. She completed her PhD in Human and Molecular Genetics at the Medical College of Virginia in 2013, where she received the Roscoe D. Hughes Award for Most Outstanding Graduating PhD candidate. Her research focused on studying the genetic etiology of novel microdeletion and microduplication syndromes identified through chromosomal microarrays by using molecular techniques such as gene expression microarrays, and ChIP-seq. She led the identification of the MBD5 gene, that is responsible for 2q23.1 deletion syndrome and 2q23.1 duplication syndrome. Following her PhD studies, Dr. Mullegama completed her postdoctoral training in the Department of Molecular and Human Genetics at Baylor College of Medicine where she worked on better understanding the phenotype of Smith-Magenis syndrome, 2q23.1 deletion syndrome, Pitt-Hopkins syndrome, and fragile X syndrome through RNA-seq pathway analysis, patient derived neural progenitor stem cells, mitochondrial assays, and sleep studies. Presently as a ABMGG Clinical Molecular Genetics Fellow at UCLA, she is involved in Clinical Exome Sequencing and NGS cancer panel research studies. Her main research interest is classifying variants by functional assays to determine clinical significance of a novel finding from Clinical Exome Sequencing to provide diagnosis to patients and their families. She has authored over 30 peer-reviewed publications, reviews and abstracts and has given numerous platform talks on her research at ASHG and ACMG conferences.

Speaker: Natalie Lippa, MS, CGC
Genetic Counselor, Institute for Genomic Medicine, Columbia University Medical Center
No financial relationships to disclose.



Natalie Lippa is a certified genetic counselor at the Institute for Genomic Medicine at Columbia University Medical Center. She currently works in genomics research with a particular focus on epilepsy and other neurologic disorders. Ms. Lippa has experience in variant interpretation, incorporating both phenotypic and bioinformatic evidence to arrive at determinations of pathogenicity. Ms. Lippa received her Bachelor of Science degree from the University of Guelph and completed her Master of Science degree in Genetic Counseling at the Mount Sinai School of Medicine. Prior to joining Columbia, she was a Genetic Counselor at the Mount Sinai School of Medicine in a specialty metabolic clinic, specializing in research projects related to PKU and Niemann-Pick types A and B disease.

Speaker: Sujatha Sastry, MS, CGC
Genetic Counselor, GeneDx
Financial relationships to disclose. (Self): Employee of GeneDx, Inc., a wholly-owned subsidiary of OPKO Health Inc.



Sujatha is a board-certified genetic counselor with more than 20 years of experience. She has been part of the Neurogenetics team at GeneDx since 2016. Prior to joining GeneDx, Sujatha was a clinical genetic counselor at Children's Hospital of Michigan where she provided pediatric and adult genetic counseling services. She also served as the coordinator of the Lysosomal Storage Disease Treatment Program. The first 9 years of her career were spent providing prenatal, pediatric, neurogenetic and cancer genetic counseling services in New York. Sujatha holds a Master of Science in genetic counseling from the University of California- Berkeley.

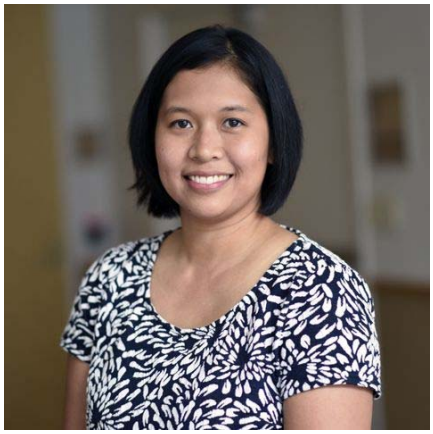
Speaker: Andrea Gonzalez Mantilla, MD
Postdoctoral fellow, Autism & Developmental Medicine Institute, Geisinger Health System
No financial relationships to disclose.

Dr. Andrea Gonzalez-Mantilla is a Postdoctoral fellow at the Autism & Developmental Medicine Institute (ADMI) at Geisinger Health System in Lewisburg, Pennsylvania. Her most recent work has been focused on the annotation, classification, and analysis of structural and sequence pathogenic loss-of-function variants in individuals with developmental brain disorders, such as intellectual disability, autism, schizophrenia, epilepsy, bipolar disorder, and ADHD. Dr. Gonzalez-Mantilla's research is also aimed at exploring the overlap between apparently different developmental brain disorders in order to identify common etiological genes and pathways. She is one of the founders and curators of the developmental brain disorder gene database.

Speaker: Anne Slavotinek, MBBS, PhD, FACMG
Professor, Department of Pediatrics, Division of Genetics, UCSF, University of California, San Francisco
No financial relationships to disclose.

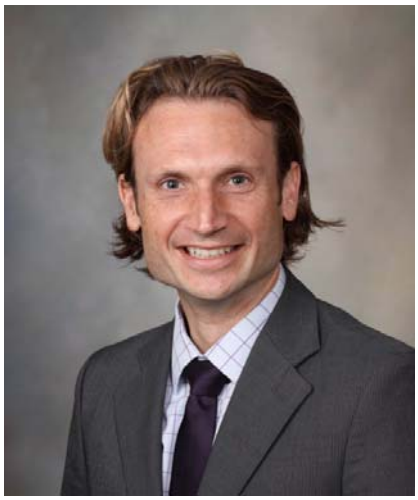
I am a Clinical Geneticist with an interest in birth defects and multiple congenital anomaly syndromes.

Speaker: Teresa Santiago-Sim, PhD
Clinical Molecular Genetics Fellow, Department of Molecular and Human Genetics, Baylor College of Medicine, Baylor College of Medicine
Financial relationships to disclose. (Self): The Department of Molecular and Human Genetics at the Baylor College of Medicine derives revenue from molecular genetic testing offered at the Baylor Miraca Genetics Laboratories



My long term research interests involve the discovery of and laboratory testing for DNA mutations that underlie human genetic disorders. After receiving a doctorate degree in Biomedical Science from the University of Connecticut, I pursued postdoctoral training in human genetics in Harvard Medical School under the mentorship of neurosurgeon Dr. Dong Kim, cardiologist Dr. Christine E. Seidman, and geneticist Dr. Jonathan G. Seidman. My project was focused on identifying genes that when mutated, predispose individuals to intracranial aneurysms, a common cause of subarachnoid hemorrhage. During my postdoctoral experience, I received a training fellowship award in research methodology, epidemiology, statistics and genetic approaches from the American Heart Association/Bugher Foundation Centers for Stroke Prevention. I continued to develop the aneurysm research program as Assistant Professor in the University of Texas Medical School at Houston with grant funding received from the Brain Aneurysm Foundation, American Heart Association and the National Institutes of Health. The aneurysm study led to identification of rare pathogenic variants in the THSD1 gene, showed that THSD1 loss could result in cerebral bleeding in animal models, and provided evidence for a role of THSD1 in endothelial cell adhesion. To pursue my passion for mutation discovery and desire to work in a clinical setting, I am currently in training to become a Clinical Molecular Geneticist in Baylor College of Medicine.

Speaker: Devin Oglesbee, PhD
Department of Laboratory Medicine and Pathology, Mayo Clinic
No financial relationships to disclose.



Participation Instructions

1. Participant logs into ondemand.acmg.net
2. Once logged in the participant will access the session they would like to view. They will be asked if they would like to claim credit for the meeting, or if they will not claim credit for the meeting. Then, this information (Course description) will appear, and participant will have to attest that they have read the information. They will then click Continue.
3. After that, the participant will be able to select the credit types to claim.
4. For each session with a post-test, the participant will need to mark and complete the matching pre-test.
5. Then the participant will watch the session presentations.
6. Participant will complete viewing all session content. "Check marks" indicate which presentations have been viewed.
7. After viewing all presentations within a session, participant will click the "Claim Credit for Session" button under the CME dropdown at the top of the page.
8. Participant should take and then successfully pass the post-test. If they do not pass with a score of 80% or higher, they will have unlimited tries to pass the post-test.
9. Participant will continue the steps above to earn credits for additional sessions.
10. If a session does not have a test attached, the participant will not need to take a pre- or posttest, but will have to complete a Concurrent or Plenary session-specific evaluation to claim credit.
11. To print their certificate, the participant will click the "Print Certificate" button under the CME dropdown at the top of the page. Participant must complete the meeting evaluation (one time only) before they can access their certificate. Participant will then choose their certificate(s). The certificate(s) will be automatically updated as they earn new credits.

Stream Requirements	
Network	For best results, use a hardwired network connection instead of wireless
Full Screen Viewing	If you would like to view the webcast full screen, display the tool bar at the bottom and click the double arrow in the far right corner. The screen will enlarge to the full screen of you system. To restore the size, press the "ESC" key
Refresh Browser Window	If the webcast freezes and does not recover in 3-4 seconds, refresh browser window
Freezing or Stuttering Issues	Adjust the amount of bandwidth needed by putting your mouse anywhere over the video window. A tool bar will appear at the bottom. On the right side you will see a "HD" button, click on that button and you will see a list of options. The top is "auto", with decreasing numbers below. Select a lower bandwidth (such as 360p) to see if your webcast improves

For Technical Support call	1-800-504-5379

Mobile Viewing Requirements

Android Devices	Android 2.3+ with Adobe Flash Player 10.2 or better installed Install Flash Player
Apple Devices	iOS 4+

Online Viewing Requirements

Bandwidth	512kbps
Required Hardware and Software	Screen resolution of 1024X768 or larger Sound card and speakers/headphones
Browser	Microsoft Internet Explorer 7.0 or better Mozilla Firefox 4 or better Safari 5 or better
Windows	Operating System: Windows 8 desktop mode, Windows 7; Windows Vista; Windows XP Service Pack 2 or 3 x86 or x64 (Browsers must be in 32-bit mode) 1.6-gigahertz (GHz) or higher processor 512MB of RAM
Mac OS	Operating System: Apple Mac OS X 10.4.8 or above Intel Core™ Duo 1.83GHz or faster processor 512MB of RAM

Registration and Fees

ondemand.acmg.net
ACMG Members and ACMG Trainees: ($50)
Non-members ($60)
Additional fee (~$25) applies for NSGC credit that is billed by NSGC.

Questions regarding CE credit should be directed to education@acmg.net.

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