2017 | ACMG Annual Clinical Genetics Meeting

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

Bedside to Bench and Back: Translational Medicine in Epilepsy Genetics

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

Date of Release: April 3, 2017s
Expiration Date: April 3, 2020 (CME, NSGC, P.A.C.E.®)
Estimate Time of Completion: 1.5 hours
Course must be completed by the expiration dates

COURSE DESCRIPTION

The epilepsies are among the most common neurological conditions, affecting approximately 1% of the general population and are most common in childhood, affecting approximately 70 out of 100,000 children under the age of two years. Seizures are commonly encountered in the genetics clinic, as they are a common comorbidity of many known Mendelian disorders and many epilepsy syndromes have a strong genetic component. Recent data show that de novo alterations play an important role particularly in the early-onset epileptic encephalopathies.

Treatment for the epilepsies may be directed by seizure type, and many patients try multiple medications until they find one, or a combination of several, that help control seizures. In one of out every three people with epilepsy, seizures remain uncontrolled despite multiple medications. In some patients, the identification of the underlying molecular etiology can have therapeutic implications, leading to more targeted therapies. Recent technological advances in gene sequencing have led to a rapid increase in genes leading to epilepsies, particularly severe epilepsies of childhood. However, despite the success in gene discovery, the ability to provide targeted therapies has not paralleled this influx. The field of epilepsy genetics has now shifted efforts from focusing solely on gene discovery to investigating the mechanisms of seizure susceptibility and identifying targeted therapies in the laboratory that can be translated back to the clinic. In this session, we will present a translational approach to the diagnosis, providing examples of how gene discovery in the epilepsies has led to a better understanding of the underlying mechanisms, forming a basis for precision medicine.

During this session, we will have four speakers covering topics of translational epilepsy genetics. The first speaker will provide a comprehensive clinical overview of the genetic epilepsy syndromes, including important features relevant to the pediatric genetics clinic. The second speaker will discuss current available testing options for patients with epilepsy, including next generation panel testing and whole exome sequencing, the clinical utility and diagnostic yield, and challenges in variant interpretation in the context of the epilepsies. The third speaker will discuss current translational studies and clinical trials harnessing genetic diagnoses to forge a path for precision medicine. This talk will cover many of the ongoing clinical trials for genetic epilepsies and outline the overall framework for future drug development. The fourth speaker will discuss functional analysis of identified genetic variants and screening of potential antiepileptic medications in zebrafish models of genetic epilepsies. This talk aims to present the spectrum of screening model systems for genetic epilepsies and will demonstrate how pathogenic variants identified in patients can be used for compound screening, allowing for rapid discovery of new compounds targeted at specific genetic epilepsies.

Dr. Jeremy Ullmann (Drug Screening in Zebrafish as a Model System for Genetic Epilepsies) declined to release his slides but you will be able to listen to his presentation.

LEARNING OBJECTIVES

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

- Identify current gaps in knowledge that make obtaining a definitive genetic diagnosis in epilepsy particularly challenging
- Outline efforts to provide functional analysis for variants in genes associated with epilepsy as well as efforts for drug-screening in animal models
- Describe how findings have translated back to the clinic to inform patient care and how such efforts need to be expanded
- Describe ongoing collaborative efforts in clinical research relevant for patients with seizure disorders

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

- Seizures in the Genetics Clinic: A Comprehensive Update of Genetic Epilepsy Syndromes- Ingo Helbig, MD
- Genetic Testing in the Epilepsies: Testing Options, Diagnostic Yield, and Unique Challenges in Variant Interpretation- Amanda Bergner, MS, CGC
- Personalized Medicine Approaches to Specific Genetic Epilepsies: The 2017 Landscape-Annapurna Poduri, MD, MPH
- Drug Screening in Zebrafish as a Model System for Genetic Epilepsies: The Path to Precision Medicine- Jeremy Ullmann, PhD

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 1.5 *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 1.5 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 1.5 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

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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)

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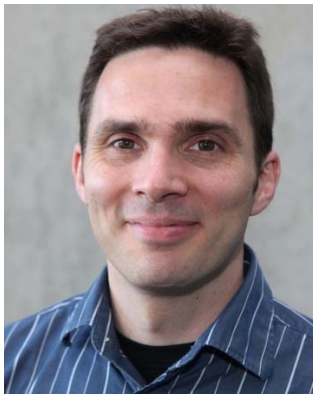
SPEAKERS AND MODERATORS

Faculty Disclosures:

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.

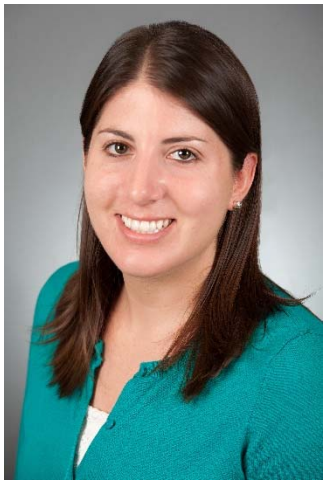
Moderator/ Speaker: Ingo Helbig, MD
Division of Neurology, The Children's Hospital of Philadelphia, Philadelphia, PA; Department of Neuropediatrics, Christian-Albrechts-University of Kiel and University Medical Center Schleswig-Holstein, Kiel, Germany.
Financial relationships to disclose. (Spouse): **Salary/Employment**: **Ambry Genetics**



Ingo Helbig, MD, is a European pediatrician and child neurologist currently working at the Children's Hospital of Philadelphia with a focus on the diagnosis and treatment of genetic epilepsies. Dr. Helbig received his clinical and

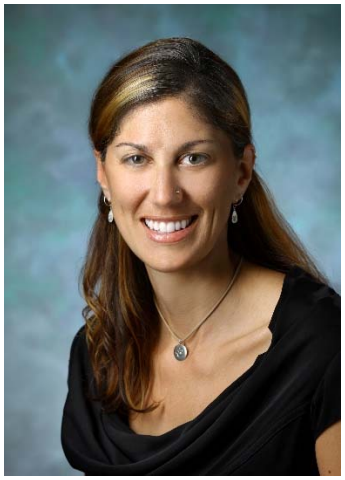
research training at the Epilepsy Research Centre, Melbourne, Australia, the Department of Neuropediatrics at the University of Kiel, and the Division of Neurology, Children's Hospital of Philadelphia. He has been involved in the discovery of microdeletions as genetic risk factors for epilepsy and has recently co-chaired the European EuroEPINOMICS-RES consortium, a European collaboration involved in many of the recent gene findings for severe epilepsies. He is currently member of the Genetics Commission of the International League Against Epilepsy and member of the ClinGen pediatric neurology clinical domain working group. Ingo is writing about epilepsy and genes on Beyond the Ion Channel, a scientific blog dedicated to epilepsy and genes.

Moderator: Lacey Smith, MS, CGC
Licensed Genetic Counselor, Division of Epilepsy and Clinical Neurophysiology, Boston Children's Hospital
No financial relationships to disclose.



Lacey Smith, MS, CGC is a Licensed Genetic Counselor in the Epilepsy Genetics Program at Boston Children's Hospital. She provides genetic counseling services to patients and families seen in the Epilepsy Genetics Clinic. In addition to her clinical role, she coordinates the PCDH19-related epilepsy patient registry and assists in ongoing research efforts surrounding gene discovery in epilepsy. Lacey is one of the founding members of EpiGC, an international network of genetic counselors who specialize in epilepsy genetics and who are dedicated to the education of both providers and families, and is the chair of the Consumer Outreach Committee within EpiGC.

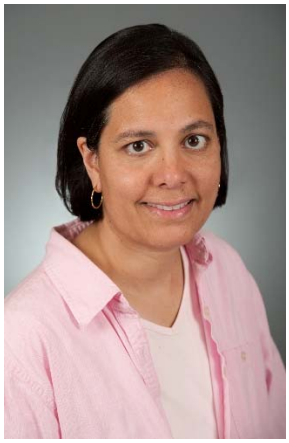
Speaker: Amanda Bergner, MS, CGC
Senior Product Manager, Neurology, Ambry Genetics
Financial relationships to disclose. (Self): Salary/Employment: Ambry Genetics



Amanda Bergner received a B.A. in Psychology and Environmental Science at the University of Virginia and an M.S. in Genetic Counseling from the University of California, Berkeley. Ms. Bergner began her career at the National Fragile

X Foundation providing genetic counseling and educational services for families living with fragile X and related conditions. In 2001, she moved to clinical care at Johns Hopkins in General Genetics with a focus on neurometabolic diseases. In 2008, Ms. Bergner became the first genetic counselor in the Neurology Department at Johns Hopkins, working primarily in the Comprehensive Neurofibromatosis Center, which she co-founded in 2003. She began conducting clinical research regarding the process of adaptation of individuals and families to chronic, inherited disease and transitioned to a faculty position as an Assistant Professor of Neurology and Genetics. Her clinical work expanded along with the growth of the field of neurogenetics and she provided genetic counseling services within several subspecialty clinics: ataxia, pediatric neurogenetics/epilepsy, neuromuscular disease, and ALS. Throughout her career, Ms. Bergner has educated genetic counseling students, through clinical rotations and observations, as well as serving on the faculty for the NHGRI/Johns Hopkins Genetic Counseling Training Program. She is currently a board member of the Accreditation Council for Genetic Counseling (ACGC) and is on the faculty of the Sarah Lawrence Genetic Counseling training program. Ms. Bergner joined Ambry Genetics in 2015 as the Senior Product Manager focused on Neurology genetic testing.

Speaker: Annapurna Poduri, MD, MPH
Associate Professor of Neurology, Harvard Medical School, Epilepsy Genetics Program, Dept. of Neurology, Boston Children's Hospital
No financial relationships to disclose.



Dr. Poduri directs the Epilepsy Genetics Program as a clinician-scientist, with one hand in the clinic as a pediatric epileptologist and the other hand in the laboratory on a mission to identify the genetic underpinnings of epilepsy. At Boston Children's Hospital, she is also the Co-Director of the Neurology Department's Program in Neurogenetics and serves on the BEST Committee for standardizing laboratory practices. Dr. Poduri is a key participant in epilepsy genetics research at the local and national levels. She has been an Epilepsy Genetics Benchmark Steward to the National Institute of Neurological Disorders and Stroke (NINDS) and the Boston Children's Principal Investigator for the NIH-funded Epilepsy Phenome/Genome Project (EPGP), a national, multi-centered research study. She has been actively involved in data quality review and publications from the phenotyping phase of that project, and is now involved in the genotyping phase. Dr. Poduri's post-doctoral work focused on familial epilepsies as well as somatic mutations in epileptic brain malformations. She is part of an international effort to understand the genetics of severe early-onset epilepsies and continues to study the genetics of brain malformations, including post-zygotic mutations. Her laboratory has begun to model epilepsy genes in the zebrafish system with a vision to contribute pre-clinical work to precision medicine efforts in epilepsy research. Ultimately, she plans to take this research back to the clinic through the clinical arm of the Epilepsy Genetics Program.

Speaker: Jeremy Ullmann, PhD
Research Fellow, Department of Neurology, Boston Children's Hospital and Harvard Medical School
No financial relationships to disclose.

Dr. Ullmann is a neuroscientist with extensive experience in imaging and zebrafish models of neurodegenerative disease. He received his BSc in Biology from Brandeis University in 2003 and a PhD in neuroscience and Imaging at The University of Queensland in Brisbane Australia in 2010. He completed his first fellowship at the Centre for Advanced Imaging (The University of Queensland) under Prof. David Reutens where he developed the world's highest high-resolution models of pre-clinical animal models and examined the correlation of febrile seizures and temporal lobe epilepsy later in life. In 2016 he joined the Epilepsy Genetics Program and Boston Children's Hospital and Harvard Medical School where he is performing high-throughput genetic and drug screens on candidate epilepsy genes.

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

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ACMG Members and ACMG Trainees: ($50)
Non-members ($60)
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