

May 10, 2013

Recent Activities of The American College of Medical Genetics and Genomics

The American College of Medical Genetic and Genomics (ACMG) is the professional home to nearly 1,600 board certified clinical and laboratory genetics professionals and is the only nationally recognized medical organization dedicated to improving health through the practice of medical genetics and genomics. The College's mission includes the following major goals: 1) to define and promote excellence in the practice of medical genetics and genomics and to facilitate the integration of new research discoveries into medical practice; 2) to provide medical genetics and genomics education to fellow professionals, other healthcare providers, and the public; 3) to improve access to medical genetics and genomics services and to promote their integration into all of medicine; and 4) to serve as advocates for providers of medical genetics and genomics services and their patients. This report summarizes key activities of the ACMG between February and April 2013.

2013 Annual Meeting Sets New Records, Gavel Passed to Next ACMG President and Board of Directors Releases Important New Clinical Statements **2013 ACMG Annual Meeting Highlights**

The 2013 ACMG Annual Clinical Genetics Meeting was held March 19-23, 2013 in Phoenix, AZ, in conjunction with the 44th Annual March of Dimes Clinical Genetics Conference on Skeletal Dysplasias and Connective Tissue Disorders. In what appears to be a continuing trend, the meeting set several new records with growth in attendance, exhibitors, industry support and proposal and abstract submissions:

- A 4% increase in attendance accounted for 1,807 professional participants and an overall attendance of 2,334 with the inclusion of exhibitors, media personnel and guests. Nearly 400 meeting registrants arrived a day early to attend a Short Course.
- Over 500 poster presentations shared the Exhibit Hall with 182 booths representing 129 companies and organizations.
- The new meeting "mobile app" was downloaded by more than half of meeting attendees, doubling the industry average of 25%.

For those unable to travel to Phoenix, the concurrent, plenary and short course sessions are available on audio, synchronized to the speakers' PowerPoint presentations, and may be purchased as downloadable content on a computer or other device. For recorded content from the Annual Meeting please visit the Digitell ACMG ProLibraries site at www.prolibraries.com/acmg or call 800-679-3646.

Dr. Gail Herman Becomes President of the ACMG

Gail E. Herman, MD, PhD, FACMG took over as ACMG's new President, following Wayne W. Grody, MD, PhD, FACMG, who completed his two-year term at the 2013 Annual Clinical Genetics Meeting. Dr. Herman earned a PhD in Biochemistry and her MD degree through the NIH-funded Medical Scientist Training Program at Duke University. She completed residency training in Pediatrics and a fellowship in Genetics at Baylor College of Medicine, Houston, TX and joined the faculty at what is now the Department of Molecular and Human Genetics, Baylor College of Medicine in 1988. In 1997, Dr. Herman joined the Department of Pediatrics at Nationwide Children's Hospital and Ohio State University, where she is a tenured professor. She served as Director of the Division and Center for Molecular and Human Genetics in the Department of Pediatrics from 1998 to 2009, and currently divides her

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time between her clinical practice of pediatric genetics and basic molecular genetics research. She is an internationally recognized expert on disorders of cholesterol biosynthesis. Dr. Herman's research has recently extended to the genetics of autism spectrum disorders, serving as PI on a large multisite project funded by the Department of Defense to develop a local registry of autism families and to identify autism susceptibility genes.

As President-Elect, Dr. Herman helped the ACMG develop guidelines and best practice policies and procedures to keep up with the pace of the evolving technologies engulfing medical genetics. During her term as President, Dr. Herman intends to maintain the College's position at the forefront of promulgating clinical and laboratory practice recommendations and defining policy. She also plans to continue the College's efforts in education, training and attracting new students into the field of medical genetics.

Five Directors retired from the ACMG Board in 2013 and were thanked for their service: Rick Martin, MD, FACMG; Sue Richards, PhD, FACMG; Piero Rinaldo, MD, PhD, FACMG; Robert Saul, MD, FACMG; and Marc Williams, MD, FACMG. They are replaced by five new Directors (listed in the February 2013 Report), and by Gerald (Jerry) Feldman, MD, PhD, FACMG, Professor of Pediatrics, Molecular Genetics, Medicine, and Pathology and Director of Clinical Genetics Services at Wayne State University School of Medicine, who began a two-year term as President-Elect.

Highly-Anticipated Recommendations on Incidental Findings in Clinical Exome and Genome Sequencing Now Available, Along with A Follow-up Commentary

During its March 19th meeting, the ACMG Board of Directors approved and subsequently released its landmark document, "ACMG Recommendations for Reporting of Incidental Findings in Clinical Exome and Genome Sequencing." The 27-page report (attached) was developed through a yearlong consensus process by a Working Group comprised of medical and laboratory geneticists, with critical input from outside reviewers. The report includes detailed recommendations as well as the background and rationale for these recommendations. Robert C. Green, MD, FACMG, a medical geneticist at Brigham and Women's Hospital and Harvard Medical School co-chaired the Working Group with Leslie G. Biesecker, MD, FACMG, chief of the Genetic Disease Research Branch at the National Human Genome Research Institute; Dr. Green is the Report's lead author.

In the past, incidental genetic findings (unrelated to the condition for which the patient was tested) were seldom provided to the patient. However, as exome and genome sequencing become more commonly used in medical care, doctors will increasingly be able to learn about genetic changes that increase an individual's risk for developing an unrelated disease. Prior to ACMG's releasing these new recommendations, no single expert resource addressed how to handle incidental findings (IF) or provided a minimum list of conditions, genes, and variants that are recommended to be returned whenever clinical sequencing is performed. The ACMG now recommends that for the conditions on the list, the laboratory should return the IF to the doctor ordering the sequencing, and those doctors should manage this information with the patient in the context of that patient's clinical presentation and family history. It is ACMG's intent that this report will standardize the process by which the comprehensive power of genomic sequencing can be tailored to optimally benefit patients when clinically important findings not directly related to the primary reason for ordering the test are revealed. The short list in the report represents well-understood conditions/genes/variants for which the possibility exists of medical intervention with high benefit to the health of those carrying the variants—and their blood relatives—if they are detected pre-symptomatically. It is anticipated that a small percentage of families that are sequenced, perhaps only 1-2%, will learn unexpected but potentially life-saving information about an illness for which they may have never suspected they were at risk.

The report concludes: "In summary, the Working Group has recommended that when a report is issued for clinically indicated exome and genome sequencing, a minimum list of conditions, genes and variants should be routinely evaluated and reported to the ordering clinician who can place them into the context of that patient's medical and family history, physical examination and other laboratory testing." It further states, "The Working Group recognizes that this list should, and will, evolve as further empirical data are collected on the actual penetrance of these variants, and on the health benefits and costs that might follow from their disclosure as incidental findings." Mechanisms to update the list are currently being developed. The Full Report is also available on the ACMG website (www.acmg.net) and will be published in the July 2013 issue of *Genetics in Medicine*. It is anticipated that these recommendations will facilitate the transition to new models of delivering genomic information.

Clarifying Statement to ACMG Recommendations on Return of Incidental Findings Subsequently Issued

This week, in response to numerous commentaries in favor of and against ACMG's "Recommendations for Reporting of Incidental Findings in Clinical Exome and Genome Sequencing," the College issued a short follow-up statement addressing both misinformation and misinterpretations about the Recommendations (attached). Five issues

related to the Recommendations are addressed in the "ACMG Statement on Incidental Findings in Clinical Genomics: A Clarification." These include: 1) patient autonomy; 2) incidental findings in children; 3) clinical laboratory considerations; 4) result communication and 5) prediction of disease likelihood.

The ACMG Clarification document states, "The era of genomic medicine has begun, and we expect that it will continue to challenge long held models of medical practice. The ACMG Recommendations on Return of Incidental Findings resulting from genome sequencing represent an early step in responding to this challenge. Many issues remain to be addressed, such as billing and reimbursement for testing that includes incidental finding identification and the approach to incidental findings identified in family members who are tested to help interpret the results in a patient. We appreciate the constructive dialogue that our statement has generated and look forward to working with the medical community and the public to ensure the best and most ethical use of genomic information in medical decision-making going forward." The Clarification document can also be found at www.acmg.net in the Publications section under Policy Statements/Genomic Sequencing.

New Policy Statement on Noninvasive Prenatal Screening (NIPS) Released

ACMG has released an important new Policy Statement on "Noninvasive Prenatal Screening for Fetal Aneuploidy." The last four decades have seen many improvements to prenatal genetic screening and diagnosis. However, the inherent risks of invasive procedures (*e.g.*, amniocentesis and chorionic villus sampling) have led to an ongoing search for new methods that can provide information about the genetic status of the fetus using maternal blood specimens obtained noninvasively. The most recent advances in genomics and genomic technologies have resulted in noninvasive prenatal screening using cell-free fetal DNA (NIPS). The acronym NIPS is used in ACMG's Statement to emphasize the screening nature (false positives and false negatives do occur) of tests currently on the market. The new ACMG Statement on Noninvasive Prenatal Screening addresses: 1) the current advantages and limitations of NIPS; 2) the advantages of NIPS compared with current screening approaches; 3) pretest and posttest genetic counseling; 4) the reporting of results by laboratories performing NIPS; and 5) oversight of analytical and bioinformatic components of testing by laboratories performing NIPS. The Statement says that while studies are promising and demonstrate high sensitivity with low false-positive rates, limitations to NIPS remain. Therefore, the College strongly recommends that positive results should be followed-up with an invasive diagnostic test before any decisions are made regarding pregnancy termination. Obstetric care providers are urged to become familiar with the advantages and disadvantages of NIPS, and they should provide patients with both pretest and posttest counseling with the goal of avoiding patient harm or confusion. The Statement can be found in the Publications section of the ACMG website at www.acmg.net (Policy Statements/Prenatal Screening) and will soon be published in *Genetics in Medicine*.

ACMG Publishes Recommendations on Risk Categorization for Lab-Developed Tests for Inherited Conditions

A new ACMG Policy Statement, "Risk Categorization for Oversight of Laboratory-Developed Tests (LDTs) for Inherited Conditions," was published in the April issue of *Genetics in Medicine*. The Statement was developed by a joint working group of the Laboratory Quality Assurance and the Professional Practice and Guidelines Committees of the College and can be accessed on the ACMG website (www.acmg.net) under Publications/Laboratory Standards and Guidelines/Risk Categorization. Risk classification has been among the determinants of how medical tests are overseen and regulated by the US Food and Drug Administration (FDA). Therefore, as LDTs for germ-line (*i.e.*, inherited) mutations continue to proliferate without sound regulatory frameworks in place, the workgroup considered the medical risks and implications resulting from germ-line mutation analysis in a variety of contexts to develop the proposed approach. ACMG expects the expert opinion represented in the proposed classification system to be used to guide federal agencies, policymakers and other stakeholders.

ACMG categorized testing for inherited conditions in a three-tiered risk-based system, as recommended by the College of American Pathologists (CAP) and consistent with the usual FDA determination of testing-associated risk, whereby FDA aligns risk with the medical decision made on the test results. ACMG's proposed risk categorization model is based on how an incorrect result might impact patients and their blood relatives (including offspring). The risk model specifies determining factors for categorization and recommendations for oversight and test interpretation for low, moderate and high levels of risk. The recommendations also recognize that genetic testing is a process that includes not only the analytical phase, but also pre-analytical and post-analytical components, which are beyond the scope of the document. Due to the potentially serious implications of an incorrect result or interpretation for the patient and the patient's blood relatives, the statement recommends that an individual certified in Clinical Genetics (ABMG), Clinical Cytogenetics (AMBG), Clinical Molecular Genetics (ABMG), or Molecular Genetic Pathology (ABPath/ABMG) should provide the professional interpretation of test results. In addition, we recommend that an

ABMG certified Clinical Geneticist and/or ABGC/ABMG certified Genetic Counselor provide pre- and post-test counseling to patients, as necessary.

Newly Revised Interactive Educational Tool Demonstrates How Genetics is the Future of Medicine

Experience the Future: Discover the Power of Genetics (2nd ed.), now available from the National Coordinating Center for the Regional Genetic Services Collaboratives (NCC) and ACMG, is the ideal resource for genetics educators who are seeking an innovative, experiential approach to reach students and conference audiences, and who aspire to assure that “genetic and genomics are the future of medicine” is their take-away message. *Experience the Future: Discover the Power of Genetics* introduces participants to the experience of discussing genetic information and receiving genetic test results through live, simulated counseling encounters with experienced genetic counselors and medical geneticists. The newly revised curriculum is comprised of seven disease-specific modules (colon cancer, cystic fibrosis, fragile X syndrome, hereditary breast-ovarian cancer, hemochromatosis, multiple endocrine neoplasia type II and sickle cell disease), and each module provides all necessary program materials for both faculty and participants. There is also a detailed User’s Guide. The curriculum is suitable for use with medical students, residents, and all other types of health professionals, either as part of primary training at the undergraduate and graduate levels or as continuing education. All program materials are for sale on a flash drive, for \$35, with \$5 added for shipping. For more information please contact Sophie Stich at [sstich@acmg.net](mailto:ssstich@acmg.net).

The 2012 revision of *Experience the Future: Discover the Power of Genetics* was supported by the National Coordinating Center for the Regional Genetic and Newborn Screening Service Collaboratives (NCC), cooperative agreement U22MC03957, between the Maternal and Child Health Bureau/Health Resources and Services Administration, Genetic Services Branch, and the American College of Medical Genetics and Genomics.

90 NBS Stakeholders Participate in NBSTRN Network Meeting to Lay Groundwork for Next Phase of Work

On April 8-9 the Newborn Screening Translational Research Network (NBSTRN), which is funded by a contract from the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NIH) to ACMG, convened a breadth of stakeholders—from NBS researchers to state public health/NBS program professionals, policymakers, and advocates—to lay the groundwork for the next phase of work. The Program included demonstrations of the tools and resources offered through the NBSTRN (see February 2013 ACMG Report), updates on NBS pilots for SCID, LSD, SMA and muscular dystrophy, robust discussions of new technologies and the use of whole genome sequencing in the context of NBS, reports from NBSTRN grantees, consideration of ethical, social and legal issues, and an overview of available NIH resources. (Now in its fifth year, the NBSTRN works to improve the health outcomes of newborns with genetic or congenital disorders by means of an infrastructure that allows investigators access to robust resources for newborn screening research). Information about all NBSTRN programs can be found at www.nbstrn.org; presentations from this meeting can be found at <https://www.nbstrn.org/node/254>.

ACMG Foundation for Genetic and Genomic Medicine Updates

Three ACMG Foundation Awardees Announced at March 2013 Annual Meeting

Lindsay C. Burrage, MD, PhD of Baylor College of Medicine/Texas Children’s Hospital and Shane C. Quinonez, MD of The University of Michigan were selected as the 2013-2014 recipients of the **Genzyme/ACMG Foundation Medical Genetics Training Awards in Clinical Biochemical Genetics**. The objective of the Genzyme/ACMG Foundation Awards is to support a national training program that encourages the recruitment and training of clinicians in the field of clinical biochemical genetics and especially in the diagnosis, management and treatment of individuals with metabolic diseases. The Award grants each recipient \$75,000 to support one year of the trainees’ clinical genetics subspecialty in biochemical genetics following residency, allowing each recipient to participate in a unique, in-depth clinical and research experience at a premier medical center with expertise and significant clinical volume in the area of biochemical genetics. Recipients are selected by the ACMG Foundation, through a competitive process.

Dr. Burrage is currently in her second year of residency in Medical Genetics at Baylor College of Medicine. She completed her MD and PhD at Case Western Reserve University School of Medicine in Cleveland, OH and a Pediatrics Residency at Rainbow Babies and Children’s Hospital, Cleveland, OH. Her research during the Award period will involve a randomized clinical trial to evaluate the utility of sodium phenylbutyrate as a therapeutic agent in Maple Syrup Urine Disease. The second award recipient, Dr. Quinonez, received his MD from the University of Michigan, where he also completed his residency in Pediatrics and began his residency in Medical Genetics in 2011. His research focuses on Cystinosis and the potential correction of cystine storage via microvesicles. He will continue his training as part of the Clinical Biochemical Genetics Program.

Caleb P. Bupp MD was also honored as the 2013 recipient of the **ACMG Foundation/ Signature Genomics from**

PerkinElmer, Inc. Travel Award for his platform presentation, *Twenty years of neural tube defect surveillance and prevention in South Carolina*. Dr. Bupp received his MD degree from the University of Toledo College of Medicine. He completed his residency in Pediatrics at the University of Louisville and is currently completing his Medical Genetics Residency at the Greenwood Genetics Center, Greenville, SC. The ACMG Foundation/Signature Genomics Travel Award is given to an ACMG Trainee Member whose abstract submission was chosen as a platform presentation during the ACMG Annual Clinical Genetics Meeting. The ACMG Program Committee selects the Travel Award recipient based on scientific merit. In recognition of the selected presentation, Signature Genomics covers the travel costs for the recipient to the ACMG meeting.

Orr Associates Selected to Handle Fundraising for ACMG Foundation

The ACMG Foundation recently announced that it is outsourcing its development/fundraising functions in order to better carry out the Foundation Board’s 2013 strategic objectives. After a detailed search by a Foundation subcommittee, Orr Associates (OAI) was selected to fill this need. OAI is based in Washington, DC and has assigned a five-person team of consultants to work with the ACMG Foundation Staff and Leadership, both from their offices and onsite in Bethesda. OAI’s five-phase approach will include Orientation, Assessment, Market Study, Fundraising and Evaluation.

Ten Future Medical Geneticists to Participate in ACMG Foundation's 2013 Summer Genetic Scholars Program

The ACMG Foundation for Genetic and Genomic Medicine is pleased to announce that generous industry support has enabled the 2013 Summer Genetic Scholars Program (SGSP) to get underway. One scholar at each of ten institutions recently was selected as a participant for 2013. Thanks go to Amicus Therapeutics and to the ACMG for making SGSP a reality for its third consecutive year. Support for SGSP is included in the revised fundraising efforts by the Foundation, with the intention of expanding the Program to cover deserving medical students at additional institutions in 2014 and future years. A list of the 2013 participating institutions is in the table below.

| Institution | Location |
|---|-------------------|
| Genomics Institute, MultiCare Health | Tacoma, WA |
| Nationwide Children’s Hospital | Columbus, OH |
| Oregon Health & Science University | Portland, OR |
| University of California - San Francisco | San Francisco, CA |
| University of Maryland School of Medicine | Baltimore, MD |
| University of North Carolina - Chapel Hill | Chapel Hill, NC |
| University of Oklahoma Health Sciences | Oklahoma City, |
| University of Pittsburgh | Pittsburgh, PA |
| University of Washington | Seattle, WA |
| University of Texas Health Science Center at Houston | Houston, TX |

Genetics in Medicine Updates

The following Clinical and Laboratory Practice Guidelines and ACMG Policy Statements were published in *Genetics in Medicine* between February and April 2013:

Hickey SE, Curry CJ and Toriello HV. **ACMG Practice Guideline: lack of evidence for *MTHFR* polymorphism testing.** *Genet Med* 15 (2):153-156 (February 2013)

Rehder CW, David KL, Betsy Hirsch B, Toriello HV, Wilson CM and Kearney HM. **American College of Medical Genetics and Genomics: standards and guidelines for documenting suspected consanguinity as an incidental finding of genomic testing.** *Genet Med* 15(2):150-152 (February 2013)

Ross LF, Saal HM, David KL, Anderson RR, the American Academy of Pediatrics and the American College of Medical Genetics and Genomics. **Technical report: ethical and policy issues in genetic testing and screening of children.** *Genet Med* 15(3):234-245 (March 2013)

Monaghan KG, Benkendorf J, Cherry AM, Gross SJ, Richards CS, Sutton VR and Watson MS; a joint working group of the Laboratory Quality Assurance and the Professional Practice and Guidelines Committees of the American College of Medical Genetics and Genomics. **Risk categorization for oversight of laboratory-developed tests for inherited conditions.** *Genet Med* 15 (4):314-315 (April 2013)

Upcoming ACMG Genetics and Genomics Review Course Now Offers On-Site and Webinar Options

The ACMG Genetics and Genomics Review course is a popular 2-½ day intense learning environment with exam preparation lectures that cover a broad range of genetics and genomics topics presented by recognized experts in the field. The 2013 Course, to be held June 20-23, will offer participants two options—either to attend on-site at the Center for Advanced Learning and Medical Simulation (CAMLs) in Tampa, FL or via a live streaming webinar.

The webinar option will enable participation in either the (live) real-time or archived program from ones office or home via the Internet, with access to the archived program being available 24/7 for up to 24 months. The format of the webinar will be live video streaming with accompanying PowerPoint slides and a digital syllabus for each topic and session. Access to the webinar is not limited and registration for this option will be available up to the start of and following the course. For more information, contact acmgmeeting@acmg.net.

ACMG Returns to Nashville, Tennessee for the 2014 Annual Clinical Genetics Meeting

ACMG returns to Nashville, Tennessee's brand new Music City Center, March 25-29, 2014 for its Annual Clinical Genetics Meeting. The Preliminary Meeting Announcement and Call for Abstracts will be sent in October. All meeting information, online registration, housing and abstract submission materials will be available on the ACMG meeting website, www.acmgmeeting.net, at that time. Abstracts are due on December 6, 2013.

Further information about all ACMG activities and a full listing of our press releases and clinical genetics laboratory and practice guidelines can be found on our website at www.acmg.net. The ACMG website now houses an Online Learning Center, as well. ACMG uses Facebook, LinkedIn, YouTube, and Twitter to augment its educational and advocacy missions, provide news and resources related to medical genetics, and improve communication with and among its members and stakeholders.

Submitted by Michael S. Watson, PhD, FACMG

ACMG Liaison to the National Advisory Council for the National Human Genome Research Institute, NIH