February 1, 2016

Recent Activities of
The American College of Medical Genetics and Genomics

The American College of Medical Genetic and Genomics (ACMG) is the only nationally recognized medical organization dedicated to improving health through the practice of medical genetics and genomics. ACMG represents over 1900 members, nearly 80% of which are board certified clinical and laboratory geneticists and genetic counselors. ACMG's mission, as redefined in the 2015 Strategic Plan, is to "develop and sustain genetic and genomic initiatives in clinical and laboratory practice, education and advocacy." Three guiding pillars underpin ACMG's activities: 1) Clinical and Laboratory Practice: Establish the paradigm of genomic medicine by issuing statements and evidence-based or expert clinical and laboratory practice guidelines and through descriptions of best practices for the delivery of genomic medicine. 2) Education: Provide education and tools for medical geneticists, other health professionals and the public and grow the genetics workforce. 3) Advocacy: Work with policymakers and payers to support the responsible application of genomics in medical practice. This report highlights key activities of the ACMG between mid-September 2015 and January 2016.

ACMG Celebrates 25 Years of Translating Genetic Discoveries into Better Patient Care

2016 marks the Silver Anniversary of the ACMG and a 25-year legacy of translating genetic discoveries into better patient care and establishing best practices in genetic and genomic medicine. The vision for a professional college dedicated to clinical genetics became a reality in 1990, when Dr. Michael Kaback, as president of ASHG, invited the late Dr. David Rimoin to chair an *ad hoc* committee to initiate the process of forming a new organization that would keep pace with the rapidly evolving application of human genetics to clinical medicine. By 1991, the American College of Medical Genetics had become a legally incorporated entity and held its first Board meeting with Dr. Rimoin as its President. Providers of genetic services and patients affected by genetic disorders could now benefit from national representation, and the ACMG positioned itself to speak on their behalf to organizations and agencies dedicated to healthcare delivery, certification, and regulatory issues. Soon, ACMG began publishing practice guidelines and policy statements, and holding annual meetings. ACMG gained representation in the AMA House of Delegates, became an accredited CME provider, initiated its own journal, *Genetics in Medicine,* and continues to have a leadership role in defining genetic and genomic healthcare.

This 25th Anniversary year is ACMG's opportunity to celebrate its many important contributions to the practice of genetics in medicine with a number of exciting activities planned to both commemorate the progress made in the past 25 years and also to look forward to the next 25 years. These will include special activities at our 2016 Annual Meeting, special publications, and of course, a special hashtag — #ACMGat25. Other activities are featured throughout this Report.

Advocacy, Policy and Practice Activities

ACMG Updates its 2008 Position Statement on Direct-to-Consumer Genetic Testing

In December 2015, ACMG's Board of Directors released an updated position statement on direct-to-consumer (DTC) genetic testing. The statement responds to the growing market in which genetic tests are being offered to consumers without the guidance of a knowledgeable medical professional by clearly delineating minimum requirements that should be in place at any company offering such tests to the public. The new statement, *Direct-to-Consumer Genetic Testing: A Revised Position Statement of the American College of Medical Genetics and Genomics,* emphasizes the importance of laboratory accreditation by the Clinical Laboratory Improvement Amendments (CLIA) program or equivalent accrediting body and the necessity of having certified genetics experts available to assist consumers in interpreting test

results that have medical implications. This is of particular importance given the increasing complexity of new genomic tests, and the need for results to be interpreted in context with medical and family history in order to provide meaningful information to patients and their families.

The ACMG statement offers education for clinicians and laboratories regarding consumer use of expanded genetic and genomic testing platforms. In addition, it seeks to assist consumers in avoiding the pitfalls of genetic testing that is conducted without the guidance of a certified genetics professional, such as "inadequate or lack of informed consent, testing without the appropriate indications for testing, selecting inadequate methods for testing or selecting the wrong test, misinterpretation of results leading to inappropriate choices for disease management or prevention and inadequate follow-up," as listed in the updated statement. To that end, the ACMG recommends that "the consumer should be fully informed regarding what the test can and cannot say about his or her health," and that "a genetics expert such as a certified medical geneticist or genetic counselor should be available to help the consumer determine, for example, whether a genetic test should be performed and how to interpret test results in light of personal and family history."

Genomic testing can now provide consumers with information about disease risk that must be interpreted within the context of other factors such as environmental exposures and additional health conditions. In addition, testing may return unexpected results that are unrelated to the original reason for testing and may affect not only the individual ordering the test, but also other family members. For these reasons, the ACMG states, "the consumer should be apprised of the potential for receiving results that can neither confirm nor rule out the possibility of disease, or unexpected results that are unrelated to the specific reason for testing, as well as the implications of genetic test results for family members." Questions consumers should ask include:

- Is the laboratory performing the test accredited by CLIA?
- Who will have access to the test results?
- Do you have board-certified genetic professionals available to me to help interpret the test results and answer my questions?
- What processes are in place to protect the results?
- What will happen to the DNA once testing is complete?
- Will the data be sold to or shared with any third parties?

The complete **ACMG Statement on Direct-to-Consumer Genetic Testing** is attached to this Report.

Laboratory Developed Test (LDT) Regulation, Oversight and Reimbursement: National Initiatives

ACMG continues to address the issues presented by FDA's new guidance on the regulation of Laboratory Developed Tests (LDTs). Many in the laboratory community consider the LDTs to be locally developed and delivered clinical procedures rather than the types of classical laboratory tests to be regulated by FDA. ACMG does not agree that FDA has been given legislative authority to regulate LDTs. Rather, it seems clear that the CLIA legislation that regulates laboratory practices has this authority at the current time.

Conversations in Washington about oversight and regulation of LDTs are now moving ahead in the House Energy and Commerce Committee and in the Senate Health, Education, Labor and Pensions (HELP) Committee with three hearings scheduled in the Senate, beginning in February. FDA would like to regulate LDTs as evidenced by their guidance; however, Congress is still working out the best way for LDT regulation and oversight to occur. The Diagnostic Testing Working Group (DTWG), which was initiated by individuals at Mayo in collaboration with devices companies and some large reference labs, has been lobbying Congressional offices with a proposal that gives primary regulatory authority over test validation to FDA. CLIA then oversees the ways by which laboratories run the validated tests over time with interpretation of test results being under the States' purview, within their role of overseeing physician practices and licensing. Beyond the question of legislative authority, ACMG has other problems with considerations about oversight of LDTs including that: 1) test interpretation is considered the practice of medicine and is exempted from FDA oversight; 2) laboratory tests are inadequately reimbursed, which leaves laboratories with little profit with which to invest the $1-2 million per year required of an average academic laboratory running 200 – 300 LDTs to be compliant with FDA oversight; this will drive costs of testing up considerably; and 3) rare disease testing presents unique issues. Current parameters of FDA's Humanitarian Device Exemptions have proven inadequate for incentivizing industry to bring these types of LDTs to market so imposing similar clinical trial requirements on LDTs seems likely to result in loss of access to some needed tests.

We also continue to monitor the implications of the **Protecting Access to Medicare Act (PAMA)** for genetic testing laboratories. It is clear that in this area of testing, reducing reimbursement to the lowest level of any payer would have significant implications for the viability of academic laboratories and the innovation required to improve genetic and genomic testing, as well as the access of patients to services.

ACMG Responds to OHRP Revisions to the Common Rule
ACMG has communicated its concerns with the proposed changes to the Common Rule. These primarily relate to requirements for opt-in consent for use of biosamples in population level screening programs such as newborn screening. Most hospitals in the United Stats lack staff and systems for obtaining informed opt-in consent. Hence, we recommend opt-out forms of consent in Public Health screening programs. ACMG has also expressed concerns that rare disease testing not be classified as research only because we can learn more about a disease from every new patient who is diagnosed.

ACMG's Dr. Anthony Gregg Testifies As Sole Witness Before Congress on Behalf on HR 3441, the "Accurate Education for Prenatal Screenings Act"
In our last Report to Council we described how ACMG's 2013 *Statement on Noninvasive Prenatal Screening (NIPS) for Fetal Aneuploidy* came to the attention of Congresswoman Jaime Herrera-Beutler, leading to ACMG's close involvement with her office by providing technical assistance for the drafting of HR 3441, the "Accurate Education for Prenatal Screenings Act," which was introduced in August and referred the Energy and Commerce Committee's Subcommittee on Health. Representative Herrera Beutler was joined by lead Democratic cosponsor, Representative Lucille Roybal-Allard (D-CA), and four additional cosponsors.

HR 3441 amends the Public Health Service Act to establish pre- and posttest education programs for patients and providers regarding cell-free DNA prenatal screening. The CDC is the HHS agency tasked with coordinating these efforts with broad input from stakeholder groups, including medical geneticists, obstetricians and other prenatal care providers, pediatricians, disability advocacy and parent groups, as well as industry. HR 3441 recognizes that NIPS has rapidly become a high volume test, being offered to a large proportion of pregnant patients and thereby shifting the rendering of a prenatal testing modality away from the experts into primary prenatal care. As such, pretest education and counseling, and some posttest education and genetic counseling, will be done by a variety of members of the prenatal healthcare team, creating a need for ongoing professional education to meet standards set forth in professional guidelines and to establish inter-professional consistency.

On December 9, 2015, only four months after the bill's introduction, the House Energy and Commerce Committee's Subcommittee on Health scheduled a legislative hearing on HR 3441, along with five additional unrelated public health bills. ACMG was invited to testify and was the sole witness called to provide technical expertise to the Subcommittee about the overall issue of NIPS as well as the specifics of HR 3441. Anthony Gregg, MD, lead author of the May 2013 ACMG Statement, represented ACMG and testified before the Subcommittee. Dr. Gregg outlined the importance of recognizing that NIPS is a screening tool, not a diagnostic test, as well as ensuring accurate pre-test and, if needed, post-test counseling. Several physician Members of Congress participated in the hearing and clearly valued Dr. Gregg's perspective. Subcommittee Members asked Dr. Gregg about the training needed to interpret tests, concerns that these screenings may become the standard of care, about whether counseling was nondirective in nature, cost to implement the education and training programs established in the bill, and about FDA approval or other means to ensure quality control of NIPS, in the context of FDA's expected actions on Laboratory Developed Tests (LDTs). Additionally, Dr. Gregg and Dr. Watson had a productive meeting with Representative Herrera Beutler following the legislative hearing. ACMG will continue to provide needed technical assistance to Congress as HR 3441 moves forward in the legislative process. Click here for the link to the webcast.

ACMG and *Consumer Reports* Collaborate on Genetic Testing Brochure
ACMG recently collaborated with the American Board of Internal Medicine Foundation and *Consumer Reports* to create a patient-oriented brochure, "Making Smart Decisions About Genetic Testing." While the information in the brochure neither constitutes a formal ACMG practice guideline, nor is it meant to be a substitute for medical advice, the brochure aims to give consumers basic useful information about genetic testing.
http://www.consumerhealthchoices.org/wp-content/uploads/2015/10/ChoosingWiselyGeneticTestsACMG-ER.pdf

Grant and Contract Updates

The Clinical Genome Resource Project (ClinGen)
ACMG has been particularly busy during the past several months, in its role as one of the NIH-supported Clinical Genome Resource (ClinGen) grantees. The ClinGen project team has made progress in the areas of curation, building the interface, and outreach and collaboration. Curation efforts have focused on finalizing the clinical validity framework and developing a semi-quantitative metric to score the clinical actionability of gene-disease-intervention triads. The ClinGen curation interface is now live and online, allowing biocurators to store evidence and systematically evaluate the clinical validity of gene-disease pairs. Successful

outreach efforts occurred at the ASHG and NSGC meetings in October 2015. These included a ClinGen workshop (presenting an overview of ClinGen tools and frameworks for curating), a public reception, a pre-conference symposium on variant interpretation, platform presentations and posters. In addition, about 360 patients have enrolled in GenomeConnect (www.genomeconnect.org), the ClinGen patient registry, which collects self-reported phenotypic data and genetic testing results. The ClinGen team has also worked hard to build collaborations with other similar initiatives. For example, the Somatic Cancer Workgroup has built a relationship with the Global Alliance for Genomics and Health (GA4GH). Plans are well under way as the ClinGen team partners once again with DECIPHER (DatabasE of genomiC varIation and Phenotype in Humans using Ensembl Resources) to hold an open meeting, June 24-26, in Cambridge, England. Further information about this meeting and other ClinGen activities can be found on the ClinGen website.

The Newborn Screening Translational Research Network (NBSTRN)

Now finishing its eighth year at ACMG, the mission of the NICHD-NIH funded Newborn Screening Translational Research Network (NBSTRN) is to improve the health outcomes of newborns with genetic or congenital disorders through an infrastructure that allows investigators access to robust resources for newborn screening research. The NBSTRN infrastructure includes three tools; the Virtual Repository of Dried Blood Spots (VRDBS), the Longitudinal Pediatric Data Resource (LPDR), and the Region 4 Stork Database (R4S). Recently, the NBSTRN launched the ELSI Advantage, a new resource for NBS researchers that addresses ethical, legal and social issues. This tool is comprised of an interactive website that contains information on IRB's, NBS related FAQ's, and templates to customize Consent Forms. Visit NBSTRN.org for more information. The NBSTRN is now working with various states on pilot studies of new conditions under consideration for addition to NSB programs. Pompe disease and MPS-II pilots are in progress.

The National Coordinating Center for the Regional Genetic Service Collaboratives (NCC)

ACMG has served as the National Coordinating Center (NCC) for the seven Health Resources and Services Administration (HRSA) Genetic Service Collaboratives (RCs) since 2004, through a cooperative agreement with HRSA. The current award period runs through May 2017. Under this award, NCC is: 1) developing a recommendation for a future framework for regional genetic service centers; 2) providing an infrastructure that strengthens communication and collaboration between the RCs, offers technical and clinical expertise as needed, and promotes and disseminates outcomes of RC activities; and 3) supporting the National Genetics Education and Consumer Network (NGECN) through its partnership Genetic Alliance. This past summer, NCC and NGECN developed national needs assessments aimed at genetics healthcare providers (NCC), public health (NCC), and consumers (NGECN). These needs assessments arose from listening sessions held by NCC and NGECN from January-July 2015 that sought to understand current issues (such as existing barriers and service delivery gaps) within the genetics community and gather information about existing regional models of care to better understand the tools and resources deployed by various systems to address a host of issues. Following completion of the needs assessments in December 2015, data analysis was performed. Findings from the needs assessments and the listening sessions informed the Regional Support Service Model (RSSM) workgroup and an advisory committee, each of which had been charged with developing recommendations for future genetic services models. The RSSM workgroup and advisory committee developed their recommendations after careful review of 25 existing regional care center models (e.g., CF Centers, the UK Regional Genetics Model, state programs, etc.). They also identified priorities from the national needs assessments. The two groups then drafted a brief that describes current gaps in services and offers solutions on how a genetics network could address these challenges. The brief outlines eight recommended models for care delivery along with corresponding pros/cons and the priorities they address. These recommendations will be open for public comment during February 2016 with a final report to be submitted to HRSA in March 2016. Instructions on how to provide comments can be found on the NCC website (here).

Genetics in Medicine Updates

Recent ACMG Publications

The following ACMG publication appears in the February 2016 issue of the College's monthly journal, *Genetics in Medicine:*

ACMG Board of Directors. **Direct-to-consumer genetic testing: a revised position statement of the American College of Medical Genetics and Genomics.** *Genet Med* 18(2):207-208 (February 2016) PMID: 26681314

GIM Website Now Houses All ACMG Statements and Guidelines

Genetics in Medicine has posted all the published ACMG Statements and Guidelines from the last 17 years on one easily accessed webpage (http://www.nature.com/gim/statements_and_guidelines_by_date.html). Authored by the Board of Directors and Committees of the College, these recommendations are all Board-approved and were designed to serve as educational resources for medical geneticists and other healthcare professionals to help provide quality medical genetics and genomics services.

GIM Podcasts

Use the URL http://feeds.nature.com/gim/podcast/current to access *Genetics in Medicine's* monthly Podcast, known as *GenePod,* to hear a live discussion of a timely (and often controversial) article from the most recent published journal. On the occasion of ACMG's 25th Anniversary, the January 2016 *Genetic in Medicine's* podcast takes a look back—and forward— with an exclusive conversation about the past and the future of the journal. Podcast director, Cynthia Graber interviews Richard King, the founding editor of *GIM,* and Jim Evans, the current Editor, regarding what's changed, what hasn't and what we can look forward to in the next 25 years.

Meetings and Education Updates

2016 | ACMG Annual Clinical Genetics Meeting
March 8-12 • Exhibits: March 9-11 • Tampa Convention Center • Tampa, FL

ACMG's Annual Clinical Genetics Meeting Returns to Tampa in March 2016

The 2016 ACMG Annual Meeting will be held March 8-12, 2016 in Tampa, FL. Recognized as one of Trade Show Executive Magazine's Fastest Growing Meetings for several years running, the ACMG Annual Meeting has become **the** place for professionals with an interest in clinical genetics and genomics research and practice to network with colleagues, meet new collaborators from related disciplines, and hear about the very latest developments. The 2016 Annual Meeting will be preceded by three short courses: *NAMA at the ACMG: The Best of the North American Metabolic Academy; Advanced Molecular Cancer Genetics: State of the Art Today and Beyond;* and *Tools and Approaches to Assess the Genetic Basis of Disease.* The meeting will also include the March of Dimes Clinical Genetics Conference, *Prader-Willi Syndrome: New Insight Into A Classic Genetic Disorder.*

Needless to say, the upcoming meeting will have all of the standard features of past meetings, such as Exhibit Theaters; Satellite Symposia; the NCC-sponsored Consumer Leader Program, which is conducted in partnership with the HRSA Regional Genetic Service Collaboratives, genetic counseling graduate students from the University of Arkansas for Medical Science and faculty experts; a series of events for trainees (students, residents and fellows), including the very popular Trainee-Mentor Luncheon; and the Genetic Counselors Luncheon. Several new events will be featured this year. We are introducing *ePosters:* For the first time, posters will be available online to registered meeting attendees both during and after the meeting. This will allow attendees to see all the posters they were unable to visit in the Exhibit Hall. The Exhibit Hall will also feature a *What's New Zone,* with a New Products Showcase to help attendees discover what's new and what's hot in the industry, all in a single location. Finally, there are now three *Diagnostic Dilemmas* sessions: Rare Knowns and Unknowns, Prenatal/Perinatal Diagnostic Dilemmas, and Adult Diagnostic Dilemmas. On-site registration is available, and all meeting information can be found on the meeting website at www.acmgmeeting.net.

ACMG's Genetics Academy Continues to Grow: New Genetics Case Conferences Announced for this Spring

ACMG GENETICS ACADEMY

With technical expertise provided by ACMG's Education and CME Committee, the Genetics Academy Learning Center continues to grow. Featuring both live programs and online content, there are genetics and genomics curricula (from webinars to Annual Meeting webcasts and MOC modules) to meet the needs of genetics and non-genetics health professionals at all practice levels.

ACMG GENOMICS CASE CONFERENCES

ACMG's very popular live, virtual Case Conferences have expanded to now include monthly **ACMG Genomics Case Conferences** and quarterly **Adult Genomics Case Conferences**. The University of Washington will host the next **Adult Genomics Case Conference,** *Adult Genetics in the Pacific NW: The View From Seattle,* on February 9, with subsequent sessions scheduled for May 10 and August 9. The next set of monthly **Genomics Case Conferences** includes presentations by GeneDx on February 17; Partners Healthcare on March 16; and the University of California, San Francisco on April 20. The live case conferences always occur from 2:00 – 3:00 PM ET. They are also archived in the ACMG Genetics

Academy.

For further details about the Case Conferences and all other Educational Offerings, access the ACMG Genetics Academy at ACMG.net/education.

The Genomics Case Conferences are supported by an educational grant from QIAGEN Bioinformatics and the Ingenuity Clinical Decision Support Platform.

ACMG Foundation for Genetic and Genomic Medicine Updates

The ACMG Foundation (ACMGF) surpassed several fundraising goals in 2015, achieving its best fundraising effort to date. This includes record numbers of Corporate Partners as well as individual donors at the Genetics Leadership Society level ($1000+). The Foundation is always highly visible at the Annual Meeting, through its mission to support, grow and sustain College activities, the field of medical genetics, and the professionals who comprise the ACMG membership. During the upcoming Annual Meeting, the ACMG Foundation will present five individuals with fellowship and training awards in clinical genetics, biochemical/metabolic genetics and translational genomic sciences, for a total of $490,000. These awards are made possible through the generosity of our partners from industry. The ACMG Foundation, together with gifts from PerkinElmer and Shire, is also the sponsor of the "Day of Caring," a signature event at each ACMG Annual Meeting, through which adaptive tricycles and bicycles (with helmets!) are given to about 20 children with genetic disorders. This is ACMG's way of giving something back to the communities where we hold the Annual Clinical Genetics Meeting. This year, the recipients of the adaptive bicycles will be from the Muscular Dystrophy Association's St. Petersburg/Tampa Chapter and the local F.R.I.E.N.D.S. Support Organization (Families Raising, Inspiring, Educating and Networking for Down Syndrome).

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